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BIOTECHNOLOGY DEVELOPMENT

mf 14 ORIGINAL

HEARING

BEFORE THE

SUBCOMMITTEE ON
OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON
ENERGY AND COMMERCE
HOUSE OF REPRESENTATIVES

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BIOTECHNOLOGY DEVELOPMENT

WEDNESDAY, DECEMBER 18, 1985

House of Representatives,
Committee on Energy and Commerce,
Subcommittee on Oversight and Investigations,
Washington, DC.

The subcommittee met, pursuant to notice, at 10:30 a.m., in room 2322, Rayburn House Office Building, Hon. Ron Wyden presiding (Hon. John D. Dingell, chairman).

Mr. Wyden. The subcommittee will come to order.

Our distinguished chairman will be joining us shortly. He was detained. I would like to read his statement in its entirety.

This is the third in a series of hearings by the Subcommittee on Oversight and Investigations inquiring into Federal policy and biotechnology. The first hearing explored the plans of the Cabinet Council Working Group and its member agencies for regulating biotechnology. We are particularly interested in the capacity to predict the consequences of releases of genetically engineered organisms to the environment.

The subcommittee learned that our currently inadequate science base can have two undesirable consequences: Under caution because it is difficult to be sure that a release is safe; or reckless action because the hazard is not understood, or is ignored. All participants agreed that research to enhance the Government's regulatory ability was needed.

The second hearing introduced the problem of "commercial orphans"—products which may be socially desirable, but do not appear profitable to industry. The subcommittee explored vaccines as an important example of a product that may not receive adequate commercial investment without Government intervention.

Today's hearing is an update and review of the status of United States biotechnology policy.

Although the subcommittee has been actively considering biotechnology and trade issues, particularly the efforts to harmonize international regulation, we are not covering these issues in today's hearing. The work of the Organization for Economic Cooperation and Development in this regard seems to be back on track—after a little coaxing—and a public document is due to be adopted in February. Until the product of the OECD expert working group becomes public, it will not be possible for the subcommittee to review the history or results in public session.

The first panel of witnesses today will permit the subcommittee to hear from the new biotechnology industry and from a scholar who is studying the relationship between the industry, universities, and the Federal Government. The firms that comprise the biotechnology industry have been very attentive to Federal policy and they now have two associations to represent their interests.

We will hear from a representative from each association on the subject of new agency regulatory proposals and the new Biotechnology Science Coordinating Committee. The committee is the creature of the administration, intended to coordinate the activities of all the agencies involved in the science and regulation of biotechnology.

As industry representatives describe the future of biotechnology and what will be developed with the new science, the subcommittee is interested in learning what uses of biotechnology are not likely to be developed by the private sector. As the subcommittee learned in reviewing vaccines, it is essential that the Government identify as soon as possible useful but neglected commercial orphans so that Government policy may encourage their development.

Both the industry representatives and Dr. Blumenthal, from Harvard's John F. Kennedy School of Government, can help the subcommittee understand the industry's commitment to basic research. What is the relationship between the research funded by industry and the research funded in universities, and how does this affect the need for Federal funding? Will all research topics be covered and all kinds of products developed? Biomedical? Food? Energy? Biodegradation of toxic wastes?

The second panel deals more directly with areas that appear to lack Federal policy. Marc Lappé, whose new book "Broken Code" deals with the promise of biotechnology, will expand the concept of commercial orphans. We hope to learn what is happening in food production, in energy, and medical products such as contraceptives.

Robert Nicholas, who has followed biotechnology policy for the Brookings Institution, will present the subcommittee with an analysis of the outlook for the development of biodegradation of toxic wastes. And Richard Novick, a pioneer in genetic engineering, will review his concerns about the new science and its contribution to the hazard of biological weapons.

The final panel, when we reconvene at 2 p.m., concerns new Federal regulatory policy as embodied in the BSCC. David Kingsbury, the first chairperson of the group will testify for the administration. The subcommittee is most concerned to learn how the administration is responding to the need for more research to improve regulatory decisions. It has been stated that the coordinating committee will not second guess agency decisions in the manner of OMB, but will it be able to help the agencies develop a sound scientific base for decisionmaking?

Dr. Kingsbury will be accompanied by Dr. John Moore from the Environmental Protection Agency. We are particularly pleased to have Dr. Moore before the subcommittee to address the problem of methods development. For any regulatory program there must be a standard set of predictive tests that are used to make decisions. Different programs have different statutes and may require different decisions from the same data, but there should be consensus among scientists about how well a certain test predicts the behavior of a chemical or organism in nature.

Thus, methods development, the creation and validation of predictive tests and the development of a consensus on their meaning, is the critical element for effective coordination of regulatory programs. The regulation of biotechnology is especially in need of predictive tests for ecological phenomena. What will happen to a genetically engineered organism and the environment into which it is introduced? Both Dr. Kingsbury and Dr. Moore will be able to report to the subcommittee on developments in this scientific base.

The subcommittee regrets the fact that Dr. James Wyngaarden, Director of the National Institutes of Health, who will be the next chairperson of the BSCC, could not join us today. We understand that he and Dr. Kingsbury are working together to develop the agenda for the BSCC.

This concludes Chairman Dingell's opening remarks. I have a brief opening statement as well, but I would like to recognize my distinguished friend and colleague from Minnesota.

Mr. **Sikorski**. We have followed the burgeoning development of the biotechnology industry closely. Its potential to improve the quality of human life is exciting, and we all need to work to assure that this is done. It is good, therefore, to have here today representatives of the biotechnology firms, so that we may hear their views on progress to date and on how to improve the atmosphere for creativity and for effective, positive oversight of this new industry. We realize that the industry depends heavily on Government-funded research, and I hope that today we will explore this relationship and its consequences, especially for America's economy.

We are also aware, however, of the possible harmful effects of biotechnology products in the wrong hands or in the wrong environment. We must strive for a coordinated regulatory structure based on sound scientific knowledge to ensure that we enjoy only the benefits of this technology which can contribute substantially to better health and a better environment for us all.

I commend the chairman for his insight and his leadership in this area, which began over a decade ago and is demonstrated again in these hearings. I look forward to hearing from all of our witnesses today.

I thank the chairman.

Mr. **Wyden**. I thank the gentleman from Minnesota. I think at this point let us suspend and we will finish opening statements after we come back from this vote and I hope our panel members will indulge us.

As Congress moves toward recess, we may have frequent recesses today. We will reconvene in about 10 minutes.

[Brief recess.]

Mr. **Wyden**. The subcommittee will again come to order.

We apologize to our distinguished panel members for the delay.

I have a very brief opening statement. I would ask unanimous consent it be submitted into the record.

It seems the primary scientific challenge of this decade is to harness the power and the potential of biotechnology. This country now has the tools to create biotechnological wonders and to use those wonders on behalf of mankind.

The task before us now is to make sure that the proper mechanisms are in place to make sure that biotechnology moves along the right paths and is in a position to contribute all that it can to our way of life.

The purpose of this hearing is to determine if we are on the right track in developing the necessary relationships and agreements between industry and the Government and developing appropriate Federal policy and the Federal regulatory systems.

In biotechnology the opportunities to improve society are boundless. There are a couple of areas that have come before the Energy and Commerce Committee that have demonstrated that very recently. One of the most promising areas is to develop new cleanup technologies, it seems to me, for the Superfund Program through biotechnology.

What we have today with respect to the Superfund Program is literally a toxic waste merry-go-round. We just move these dangerous toxic waste sites from one site to another without coming up with a permanent way to not produce these wastes and to dispose of them permanently.

With biotechnology we have that opportunity to get off the toxic waste merry-go-round and through the very good work done by the staff of the Energy and Commerce Committee, that is going to become a priority under the Superfund Program and I think is just one example of what biotechnology can contribute in this country.

The other area that we have looked at in this subcommittee that I think shows great promise is in delivering health care services to older people. This has been a particular interest of this gentleman and I think through additional research into vaccines we can go along way to deliver better quality health care at lower prices to older people and at a time when the Medicare system is really strapped for financial resources to go forward with some of the exciting things that need to be done in health care programs like preventive services, if we can contain the cost through innovations like biotechnology, and particularly an emphasis on vaccine research that can serve seniors, that clearly will be a most helpful development for older people in the years ahead.

Again, all of us on the subcommittee are particularly appreciative of Chairman Dingell's leadership. This is the third in a series of hearings on biotechnology. The subcommittee under Chairman Dingell's leadership plans to monitor these issues very carefully and I know the chairman is planning to join us just as soon as he possibly can this morning.

With that, let's go right to our first panel: Dr. David Blumenthal, Alan Goldhammer, and Warren Hyer.

It is the practice of our subcommittee by longstanding tradition to swear all witnesses. All of our witnesses have the right to counsel.

The Chair observes that a copy of the subcommittee rules is before you which is your right to have throughout your appearance before the subcommittee.

And do any of our first panel members have an objection to being sworn?

Please rise and raise your right hand.

[Witnesses sworn.]

Mr. **Wyden**. Gentlemen, we thank you for your attendance. We will make a copy of any prepared remarks you have this morning a part of the record in their entirety and if you could summarize your key concerns this morning, that will allow plenty of time for questions.

Let us begin, if we might, with you, Mr. Goldhammer.

TESTIMONY OF ALAN GOLDHAMMER, ASSOCIATE, TECHNICAL AFFAIRS, INDUSTRIAL BIOTECHNOLOGY ASSOCIATION; WARREN C. HYER, JR., MANAGING DIRECTOR, ASSOCIATION OF BIOTECHNOLOGY COMPANIES; AND DAVID BLUMENTHAL, EXECUTIVE DIRECTOR, CENTER FOR HEALTH POLICY AND MANAGEMENT, HARVARD UNIVERSITY'S JOHN F. KENNEDY SCHOOL OF GOVERNMENT

Mr. **Goldhammer**. Thank you very much, Mr. Chairman.

My name is Alan Goldhammer, and I am associate for technical affairs at the Industrial Biotechnology Association [IBA].

Before I proceed I would like to introduce you to Richard Godown, who is IBA's new executive director, sitting back there.

IBA is a trade group representing companies using new biological techniques such as recombinant DNA [rDNA], and cell fusion, to develop and market, in the United States and worldwide, a variety of novel products in several industrial sectors. A current membership roster is attached to this statement .

The impact of biotechnology, is now becoming a reality. Recently a biotechnology company received approval for marketing human growth hormone, the first such approval granted to a startup company.

A variety of other health care compounds produced by both recombinant DNA and monoclonal antibody technology are in various stages of testing. Recent clinical results on two of these, Interleukin-2 for cancer therapy and tissue plasminogen activator for the management of coronary blood clots, have been quite exciting.

Although the earliest applications of biotechnology have occurred in the human health care area, a significant impact on other commercial sectors is now being seen. New plant varieties created by genetic engineering should improve the output of American farmers.

Some of these should be ready for field evaluation this next growing season. One pesticide created by genetic engineering has been evaluated in field trials with promising results. The Environmental Protection Agency [EPA] has approved two genetically engineered microorganisms for field evaluation.

Increasing efforts are directed toward the use of modified microorganisms for pollution control. Biochemical pathways have been established for the degradation of many recalcitrant pollutants. We hope these will provide another tool to address environmental problems.

As advances in biotechnology have been proceeding at a rapid pace in both the commercial and academic sectors, it is useful to take this opportunity to explore the Government's policy role. Two principal roles have evolved for the Government.

The first is a regulatory role that is administered through various governmental agencies. Those agencies that will have direct authority over biotechnology products are the Department of Ariculture [USDA], the Food and Drug Administration [FDA], and the EPA.

The second role is to provide funds for basic research and the training of scientists. These efforts have been conducted by the National Science Foundation [NSF] and the National Institutes of Health [NIH], with an increasing role played by the USDA. Each of these Government activities has profound effects upon industry.

IBA accepts the premise that biotechnology products will be subject to Federal regulatory oversight. We spoke to this issue at a recent hearing conducted by Senator Gore and that testimony is appended to these remarks.

We agree with the Office of Science and Technology Policy's assessment, that current Federal statutes provide an adequate framework on which to build a regulatory regime. From industry's perspective, two key features are central to regulatory policy: Decisions must be made in a timely manner, and must be based on the best available science.

A recent policy decision by EPA now requires companies to submit data in support of protocols for the field testing of genetically engineered microbial pesticides. IBA has been supportive of this conservative approach. Delays in approval can, however, seriously affect the development of agriculturally important products whose field testing must be timed to the crop planting cycle.

In order to facilitate the review process it is important to develop both the capability of reviewers at the regulatory agencies as well as research programs to address questions of risk assessment.

However, the formulation of generic risk assessment protocols may be slow to develop and data must be evaluated on a case-by-case basis. It is important that the various parties, Government, industry, and the public develop a research agenda to address uncertainties in the risk assessment process.

A significant number of new companies have been established during the past 10 years whose goal is the development of biotechnology based products. Added to the already existing companies who are also engaged in such ventures, it is possible that regulatory agencies may be overwhelmed with product approval applications.

The ultimate goal of regulatory agencies is to facilitate the movement of safe products to the marketplace. Having sufficient personnel to review products is an absolute necessity to perform this function. Methods to ensure this should be taken by each agency responsible for the reviews.

Government funding agencies provide the support for basic research and manpower training. Industry uses the results of the research as well as the manpower in the applied research that leads to goods and services.

This system has worked extraordinarily well during the post-World War II years, and America has seen the creation of not only new products and technologies but jobs in industries that did not exist before.

As the industry has grown research and development expenditures within the private sector have become significant and should equal the amount of money budgeted by the Federal Government for 1985 in biotechnology. The Federal Government, however, should not use this increased allocation of resources by industry as a justification to trim the research budgets of NIH and NSF.

The applied research carried out by the commercial sector is no substitute for the federally funded basic research which has led to any of the dramatic breakthroughs in the health care field.

The decision to commercialize a specific product is complex and based on a variety of parameters. Among these are:

Size of the market, competition with existing products, and regulatory compliance issues previously mentioned.

An additional factor, pertinent to biotechnology, is the size and resources of the company. Small- to medium-size biotechnology companies must be cognizant of cash flow and may not be able to fund exploratory research if commercial prospects are uncertain.

Concern has been raised that the powerful techniques of biotechnology will not be fully utilized in those areas where there are no significant markets in the United States or other industrialized countries.

Although it is difficult to predict what individual companies are likely to do, preliminary evidence would argue that these concerns will be assuaged over time. Two examples that have been pointed to as lacking in applied research are the development of biotechnology-based vaccines for tropical diseases and the use of biotechnology for pollution control.

The amount of research for tropical diseases has increased with much of the focus upon recombinant DNA based vaccines. Significant progress has been made in this area and the level of participation by the industrial sector has increased significantly.

We would point out to the subcommittee that the present restriction against the export of drugs and biologicals not approved by our FDA is a marked disincentive to companies working in this area. Both biotechnology and pharmaceutical companies are reluctant to take such products through the lengthy and expensive regulatory system since these diseases are rare in the United States.

Legislation has been introduced in the Senate that would ease this restriction.

Recent environmental legislation has focused both on the cleanup of toxic waste dumps and the control of byproducts of manufacturing processes. Micro-organisms have been used in a variety of pollution abatement processes and these applications will continue.

The promise of biotechnology is the ability to manipulate micro-organisms to degrade or sequester specific pollutants.

Recent developments in this area from both the commercial and nonprofit sectors offer interesting solutions for some of these problems including the degradation of pesticide residues, chemical byproducts, and the removal of toxic metals from waste water.

The earliest applications of genetically engineered microbes will be in enclosed reactors for the processing of specific waste byproducts. The uses of modified micro-organisms in the environment are less well understood and field testing will be required to demonstrate efficacy as well as understand the complex ecological interactions in such settings.

At present, genetically engineered micro-organisms designed for environmental applications are subject to regulatory and legal uncertainties. We would point out that the early studies of efficacy and fate are not to be carried out on large tracts of land but on small test plots.

The final topic that we would like to discuss is the relationship between the commercial and nonprofit research sectors.

As the application of the new biotechnology became apparent in the late 1970's, a large number of companies were started to exploit the commercial aspects.

The leading research institutions were quick to realize that possible conflicts might arise, and rules governing equity participation, consulting, and industrially sponsored research were established. IBA believes these efforts protect the integrity of the university system.

As we have stressed it is Government's main role to fund basic research.

While some of the corporate-university research agreements appear to be quite large, in no case did the industrial contribution exceed 8 percent of the university's total research funding.

We would point out to the committee that universities have been involved in corporate sponsored research for many years and that without their help the development of several important products would have been delayed.

The ability to transfer technology from the research sector to the commercial sector is certainly key to maintaining America's ability to compete in a world economy. Appropriate corporate-industry relationships can markedly enhance this process without compromising the basic mission of the university, as a place of free inquiry.

IBA would like to thank the subcommittee for inviting us to participate in ths discussion. We would be pleased to answer any questions.

[The prepared statement of Mr. Goldhammer follows:]

STATEMENT OF ALAN GOLDHAMMER
ASSOCIATE, TECHNICAL AFFAIRS
INDUSTRIAL BIOTECHNOLOGY ASSOCIATION
BEFORE THE
OVERSIGHT AND INVESTIGATIONS SUBCOMMITTEE
HOUSE ENERGY AND COMMERCE COMMITTEE
WASHINGTON, D.C.
DECEMBER 18, 1985

Mr. Chairman and members of the subcommittee, my name is Alan Goldhammer and I am Associate for Technical Affairs at the Industrial Biotechnology Association (IBA). IBA is a trade group representing companies using new biological techniques such as recombinant DNA (rDNA) and cell fusion to develop and market, in the United States and world wide, a variety of novel products in several industrial sectors. A current membership roster is attached to this statement.

The impact of biotechnology, forecast in a Congressionally sponsored Office of Technology Assessment report two years ago, is now becoming a reality. Recently a biotechnology company received approval for marketing human growth hormone, the first such approval granted to a start up company. A variety of other health care compounds produced by both rDNA and monoclonal antibody technology are in various stages of testing. Recent clinical results on two of these, Interleukin-2 for cancer therapy and tissue plasminogen activator for the management of coronary blood clots, have been quite exciting.

Although the earliest applications of biotechnology have occurred in the human health care area, a significant impact on other commercial sectors is now being seen. New plant varieties created by genetic engineering should improve the output of American farmers. Some of these varieties have undergone lengthy evaluation in laboratory and greenhouse settings and should be ready for field evaluation this next growing season. One pesticide created by genetic engineering has been evaluated in field trials with promising results. The Environmental Protection Agency (EPA) has recently approved two genetically engineered microorganisms for field evaluation for the control of frost damage.

Increasing efforts are directed towards the use of modified microorganisms for pollution control. Biochemical pathways have been established for the degradation of many recalcitrant pollutants. We hope that genetic engineering techniques can enhance the performance of microorganisms, providing another tool to address environmental problems.

As advances in biotechnology have been proceeding at a rapid pace in both the commercial and academic sectors, it is useful to take this opportunity to explore the government's policy role. Two principal roles have evolved for the government. The first is a regulatory role that is administered through various governmental agencies. Those agencies that will have direct authority over biotechnology products are the Department of Agriculture (USDA), the Food and Drug Administration (FDA), and the EPA. The second role is to provide funds for basic research and the training of scientists. These efforts have been conducted by the National Science Foundation (NSF) and the National Institutes of Health (NIH), with an increasing role played by the USDA. Each of these governmental activities has profound effects upon industry.

IBA accepts the premise that biotechnology products will be subject to federal regulatory oversight. We spoke to this issue at a recent hearing conducted by Senator Gore and that testimony is appended to these remarks.

We agree with the Office of Science and Technology Policy's assessment, that current federal statutes provide an adequate framework on which to build a regulatory regime. From industry's perspective, two key features are central to regulatory policy: decisions must be made in a timely manner and must be based on the best available science.

A recent policy decision by EPA now requires companies to submit data in support of protocols for the field testing of genetically engineered microbial pesticides. IBA has been supportive of this conservative approach as an interim necessity because of uncertainties surrounding the use of such organisms in the environment. Delays in approval can, however, seriously affect the development of agriculturally important products whose field testing must be timed to the crop planting cycle.

In order to facilitate the review process it is important to develop both the capability of reviewers at the regulatory agencies as well as research programs to address questions of risk assessment. As an interim measure, agencies can supplement their expertise by the formation of expert advisory panels for the review of these early applications. EPA has used the FIFRA Science Advisory Panel for these purposes. Because biotechnology applications are being investigated in different sectors, the formulation of generic risk assessment protocols may be slow to develop and data must be evaluated on a case-by-case basis. It is important that the various parties, government, industry, and the public develop a research agenda to address uncertainties in the risk assessment process.

One further factor that is important to the regulatory responsibility is the question of adequate review personnel. A significant number of new companies have been established during the past 10 years whose goal is the development of biotechnology-based products. Added to the already existing companies who are also engaged in such ventures, it is possible that regulatory agencies may be overwhelmed with product approval applications. The ultimate goal of regulatory agencies is to facilitate the movement of safe products to the marketplace. Having sufficient personnel to review products is an absolute necessity to perform this function. Methods to ensure this should be taken by each agency responsible for the review of biotechnology products.

The roles of government and industry in technology development are closely linked. Government funding agencies provide the support for basic research and manpower training. Industry uses the results of the research as well as the manpower in the applied research that leads to goods and services. This system has worked extraordinarily well during the post-World War II years and America has seen the creation of not only new products and technologies but jobs in industries that did not exist before.

Discoveries funded by the National Institutes of Health have led to the creation of the modern biotechnology industry. As the industry has grown research and development expenditures within the private sector have become significant and should equal the amount of money budgeted by the federal government for 1985 in biotechnology. The federal government should not use this increased allocation of resources by industry as a justification to trim the research budgets of NIH and NSF. The applied research carried out by the commercial sector is no substitute for the federally funded basic research which has led to many of the dramatic breakthroughs in the health care field. IBA would view federal budget cutting in this area as counterproductive in the effort to maintain the United States as the preeminent leader in biotechnology.

The decision to commercialize a specific product is complex and based on a variety of parameters. Among these are: size of the market, competition with existing products, process economics including scale up, as well as regulatory compliance issues previously mentioned. An additional factor, pertinent to biotechnology, is the size and resources of the company. Small to medium size biotechnology companies must be cognizant of cash flow and may not be able to fund exploratory research if commercial prospects are uncertain.

There is significant commercial interest among IBA member companies in those areas outlined in the OTA report. However, concern has been raised that the powerful techniques of biotechnology will not be fully utilized in those areas where there are no significant markets in the United States or other industrialized countries. The Chairman of this subcommittee has held hearings concerning the development of products, such as orphan drugs in the past and certainly has expressed interest about the commercial viability of certain aspects of biotechnology.

Although it is difficult to predict what individual companies are likely to do, preliminary evidence would argue that these concerns will be assuaged over time. Two examples that have been pointed to as lacking in applied research are the development of biotechnology-based vaccines for tropical diseases and the use of biotechnology for pollution control.

The amount research on tropical diseases has increased with much of the focus upon rDNA based vaccines. Significant progress has been made in this area and the level of participation by the industrial sector has increased significantly.

We would point out to the subcommittee that the present restriction against the export of drugs and biologicals not approved by our FDA is a marked disincentive to companies working in this area. Both biotechnology and pharmaceutical companies are reluctant to take such products through the lengthy and expensive regulatory system since these diseases are rare in the United States. Legislation has been introduced in the Senate (S. 1848) that will ease this restriction. IBA supports this change and believes these new provisions will encourage research within the commercial sector on many of the tropical diseases that afflict third world countries.

Recent environmental legislation has focused both on the clean up of toxic waste dumps and the control of by-products of manufacturing processes. Microorganisms have been used in a variety of pollution abatement processes and these application will continue. The promise of biotechnology is the ability to manipulate microorganisms to degrade or sequester specific pollutants. Recent developments in this area from both the commercial and non-profit sectors offer interesting solutions for some of these problems including the degradation of pesticide residues, chemical by-products, and the removal of toxic metals from waste water.

The earliest applications of genetically engineered microbes will be in enclosed reactors for the processing of specific waste by-products. The uses of modified microorganisms in the environment are less well understood and field testing will be required to demonstrate efficacy as well as understand the complex ecological interactions in such settings. At present, genetically engineered microorganisms designed for environmental application are subject to regulatory and legal uncertainties. We would point out that the early studies of efficacy and fate are not to be carried out on large tracts of land but on small test plots that can be successfully managed. Therefore, we believe that these applications can proceed responsibly.

The final topic that we would like to discuss is the relationship between the commercial and non-profit research sectors. As the application of the "new" biotechnology became apparent in the late 1970s, a large number of companies were started to exploit the commercial aspects. These ventures more often than not involved participation of university researchers. At the same time several large companies were funding university research in these same areas to gauge how the technology would affect existing product lines as well as help penetrate new markets.

Each of these actions sparked controversy. Questions were raised about the free exchange of information in academia. Would university professors with equity holdings in biotechnology companies or working on research contracts from industry be unwilling to share information?

The leading research institutions were quick to realize that possible conflicts might arise, and rules governing equity participation, consulting, and industrially sponsored research were established. IBA believes these efforts protect the integrity of the university system. As we have stressed it is government's main role to fund basic research. While some of the corporate-university research agreements appear to be quite large, in no case did the industrial contribution exceed 8% of the university's total research funding.

We would point out to the committee that universities have been involved in corporate sponsored research for many years and that without their help the development of several important products would have been delayed. Universities profit from these interactions both intellectually, through relations with industrial scientists, and monetarily, a result of direct funding as well as any licensing revenue that might accrue.

The ability to transfer technology from the research sector to the commercial sector is certainly key to maintaining America's ability to compete in a world economy. Appropriate corporate-industry relationships can markedly enhance this process without compromising the basic mission of the university, as a place of free enquiry.

IBA would like to thank the subcommittee for inviting us to participate in this discussion. We would be pleased to answer any questions.

December 1985

IBA

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AMICON CORPORATION
Danvers, Massachusetts

AMOCO CORPORATION
Naperville, Illinois

BIOGEN INC.
Cambridge, Massachusetts

BIOTECHNICA INTERNATIONAL, INC.
Cambridge, Massachusetts

CALGENE, INC.
Davis, California

CALIFORNIA BIOTECHNOLOGY INC.
Mountain View, California

CENTOCOR
Malvern, Pennsylvania

CETUS CORPORATION
Emeryville, California

CIBA-GEIGY CORPORATION
Greensboro, North Carolina

COLLABORATIVE RESEARCH INC.
Lexington, Massachusetts

CPC INTERNATIONAL INC.
Englewood Cliffs, New Jersey

DAMON BIOTECH, INC.
Needham Heights, Massachusetts

THE DOW CHEMICAL COMPANY
Midland, Michigan

EASTMAN KODAK COMPANY
Rochester, New York

E.I. du PONT de NEMOURS & COMPANY
Wilmington, Delaware

EXXON RESEARCH & ENGINEERING COMPANY
Linden, New Jersey

FMC CORPORATION
Princeton, New Jersey

GENENTECH, INC.
S. San Francisco, California

GENETICS INSTITUTE, INC.
Cambridge, Massachusetts

GENEX CORPORATION
Rockville, Maryland

GIST-BROCADES USA INC.
Charlotte, North Carolina

HOFFMANN-LA ROCHE INC.
Nutley, New Jersey

IMMUNEX CORPORATION
Seattle, Washington

JOHNSON & JOHNSON
New Brunswick, New Jersey

LIFECODES CORPORATION
Elmsford, New York

MELOY LABORATORIES, INC.
Revlon Health Care Group
Springfield, Virginia

MILES LABORATORIES, INC.
Elkhart, Indiana

MOLECULAR GENETICS INC.
Minnetonka, Minnesota

MONSANTO COMPANY
St. Louis, Missouri

MYCOGEN CORPORATION
San Diego, California

PHARMACIA, INC.
Piscataway, New Jersey

PHILLIPS PETROLEUM COMPANY
Bartlesville, Oklahoma

PIONEER HI-BRED INTERNATIONAL, INC.
Des Moines, Iowa

ROHM AND HAAS COMPANY
Philadelphia, Pennsylvania

SANDOZ, INC.
East Hanover, New Jersey

SCHERING-PLOUGH CORPORATION
Madison, New Jersey

G.D. SEARLE & COMPANY
Chicago, Illinois

SHELL OIL COMPANY
Houston, Texas

SMITH KLINE & FRENCH LABORATORIES
Philadelphia, Pennsylvania

STANDARD OIL COMPANY (Ohio)
Cleveland, Ohio

TRANSGENE
Paris
France

THE UPJOHN COMPANY
Kalamazoo, Michigan

Mr. WYDEN. Thank you very much, Mr. Goldhammer.
Mr. Hyer.

TESTIMONY OF WARREN C. HYER, JR.

Mr. HYER. Mr. Chairman, and members of the Subcommittee on Oversight and Investigations. In my opening remarks, I would like to touch on four areas:

First, a brief introduction of the Association of Biotechnology Companies, and of myself, in order to provide you with some understanding of the prespective we bring to these hearings.

Second, a few brief remarks on the important role we see biotechnology eventually will play in the country's economy.

Third, in a bit more detail, I will provide some discussion on how large and small companies select those products they will develop and attempt to commercialize.

Fourth, I will enumerate several areas in which Federal policy can impact to help the United States achieve a leadership position in the world market for the products of biotechnology .

As requested by your staff, I will keep my introductory oral remarks to under 10 minutes. We have submitted more detailed written remarks for the record.

To begin then, the Association of Biotechnology Companies [ABC] is a rapidly growing trade association currently composed of over 130 members—approximately 80 biotechnology firms and 50 associated organizations. ABC has provided a list of our members with our written remarks.

At this point in time, our membership is primarily U.S. based. However, we do have increasing membership in Canada, Great Britain, Federal Republic of Germany, Australia, and even Thailand.

Our goal is to provide a forum to bring together the entire spectrum of biotechnology firms from the largest to the smallest, to work on areas of common interest and concern.

As for myself and my perspective, I have approximately 20 years experience in the area of industrial business development. I have served on the corporate staff of several Fortune 500 companies in new product, new venture, corporate development and merger, and acquisition capacities.

As head of my own consulting firm, I have worked with the management of high-technology firms in the computer, healthcare, and most recently biotechnology industries.

An important outcome of this work was the decisions concerning which products to develop and commercialize.

As you are aware, I am currently serving as the managing director of the Association of Biotechnology Companies.

Moving on to the issue biotechnology will play in the world economy I would like to make just two observations.

First we are still very early in the development of this technology. Just as no one was able in 1905 to forecast the major societal impact of the high technology automobile industry—the creation of the suburbs, shopping malls, drive through banks and fast food, and the interstate highway system—we don't have a good handle yet on the future societal impact of biotechnology.

A second observation on the eventual role of biotechnology is that the rapid acceptance of biotechnology is as much a result of our national social concerns as it is a result of scientific breakthroughs. The concern for ecology, the concept of space ship Earth, the interest in renewable resources and recycling has led our society to a shift from an emphasis on chemistry to an interest—and indeed openness to—biotechnology.

Moving along to item three, How do companies select new products?

Based upon my 20 years experience working with large and small companies, in areas as traditional and conservative as the food processing industry and as fast moving as the semiconductor, computer software, healthcare, and most recently biotechnology industries, I have found a basic consistency in how companies select new products. Somewhat oversimplifying there are three factors:

The first, market size. Companies generally want products that can influence their sales by 1 percent to 10 percent, that is, their share of the total market will be equal to 1 percent to 10 percent of their current sales. There are exceptions, of course.

The implication for the biotechnology, industry is that in order to encourage the commercialization of the entire spectrum of opportunities in biotechnology, you will want to encourage a full spectrum of different size companies.

The second item is proprietary position. Now, depending on the market, there are a wide range of methods to gain a proprietary position.

For a short lived product, such as a pet rock, simply being there first is sufficient to establish a proprietary position. By the time a competitor can tool up, the market is gone.

For others, such as consumer products, a strong brand name and an aggressive sales force is usually sufficient to establish and maintain a proprietary product position. The computer industry has been very effective in using high initial prices to recover development costs and then rapidly dropping prices to discourage the entry of competition.

There are also the traditional competitive positions based upon patents and trade secrets and what is referred to in some industries as the "regulatory patent" leadtime over a competitor who must still undergo a lengthy regulatory approval process.

The third factor in selecting a product to be developed is the availability of adequate funding to bring the product to market. In the interest of time I would make just two comments:

First, the current state of the development of commercial biotechnology is very much influenced by the availability of venture capital and public market financing. Because of the ease of "going public" with a health care product in the early 1980's, the newer biotechnology companies are heavily oriented toward the healthcare industry.

Many of the potentially important applications of biotechnology, special chemicals such as pollution control and toxic waste treatment, have not yet received venture capital funding.

Regulation enters the new product decision primarily as a cost factor—both as a cost of obtaining regulatory approval and the cost of running the company/project—salary, rent, et cetera—until regulatory approval is obtained. For example, a new biotechnology company will not enter into the development of a human pharmaceutical product unless it has developed a detailed strategy, including such sources of funding as additional equity and limited R&D partnerships, to cover the costs of obtaining regulatory approval and operating during the period of anticipated and unanticipated regulatory delay.

The fourth and final area I would like to address is a Government policy that will help the biotechnology industry to pursue a greater scope of product development. I will just list five issues. A more detailed discussion is contained in my written testimony.

One, basic research. Scientific breakthroughs do not appear in a vacuum but rather are based upon a large number of small advances, most of which have come from basic research funding. Biotechnology represents the research funding investments made through the NIH and NSF grants of the 1950's and 1960's.

Without continued governmental research funding new breakthroughs will be much longer coming.

The second is education of bioprocessing engineers. Without additional emphasis on this area of education we will soon be talking about a bioengineering gap.

The third is small business innovative research grants, also known as SABIR. A mechanism must be found to continue phase I funding during the submission and review period for phase II funding.

Fourth, product liability. Many biotechnology companies are unable to obtain coverage or afford the premiums if they can obtain coverage, the short-fall between insurance demand and coverage is $7 billion today; in 1987 it will be $47 billion. This insurance crisis is continuing.

International trade, biotechnology is an international business. The unpredictability of export controls makes many potential overseas partners wonder, "Should we joint venture with a U.S. company or with other developed countries whose trade policy is more predictable?"

The Association of Biotechnology Companies believes that ready and predictable access to legitimate foreign markets for biotechnology raw materials, inprocess components and products is key to the industry's continued growth. We have previously discussed this issue with subcommittee members and their staffs to discuss the importance of the Pharmaceutical Export Amendments of 1985 to the biotechnology industry.

Mr. Chairman and members of the subcommittee, I thank you for the opportunity to speak to you this morning. I would of course be happy to attempt to answer any questions you might have.

[Testimony resumes on p. 29.]

[The prepared statement of Mr. Hyer follows:]

Warren C. Hyer, Jr.
Managing Director
ASSOCIATION OF BIOTECHNOLOGY COMPANIES

MR. CHAIRMAN AND MEMBERS OF THE SUB COMMITTEE ON OVERSIGHT AND INVESTIGATIONS:

IN MY OPENING REMARKS, I WOULD LIKE TO TOUCH ON FOUR AREAS:

FIRST, A BRIEF INTRODUCTION OF THE ASSOCIATION OF BIOTECHNOLOGY COMPANIES AND OF MYSELF IN ORDER TO PROVIDE YOU WITH SOME UNDERSTANDING OF THE PERSPECTIVE WE BRING TO THESE HEARINGS.

SECOND, A FEW BRIEF REMARKS ON THE IMPORTANT ROLE WE SEE THAT BIOTECHNOLOGY WILL EVENTUALLY WILL PLAY IN THE COUNTRY'S ECONOMY.

THIRD, IN A BIT MORE DETAIL, I WILL PROVIDE SOME DISCUSSION ON HOW LARGE AND SMALL COMPANIES SELECT THOSE PRODUCTS THEY WILL DEVELOP AND ATTEMPT TO COMMERCIALIZE.

FOURTH, I WILL ENUMERATE SEVERAL AREAS IN WHICH FEDERAL POLICY CAN IMPACT TO HELP THE U.S. ACHIEVE A LEADERSHIP POSITION IN THE WORLD MARKET FOR THE PRODUCTS OF BIOTECHNOLOGY.

AS REQUESTED BY YOUR STAFF, I WILL KEEP MY INTRODUCTORY ORAL REMARKS TO UNDER 10 MINUTES. WE HAVE SUBMITTED MORE DETAILED WRITTEN REMARKS FOR THE RECORD.

I

To begin then, THE ASSOCIATION OF BIOTECHNOLOGY COMPANIES (ABC) IS A RAPIDLY GROWING TRADE ASSOCIATION CURRENTLY COMPOSED OF OVER 130 MEMBERS (APPROXIMATELY 80 BIOTECHNOLOGY FIRMS AND 50 ASSOCIATED ORGANIZATIONS). ABC HAS PROVIDED A LIST OF OUR

MEMBERS WITH OUR WRITTEN REMARKS. AT THIS POINT IN TIME, OUR MEMBERSHIP IS PRIMARILY U.S. BASED. HOWEVER, WE DO HAVE INCREASING MEMBERSHIP IN CANADA, GREAT BRITAIN, FEDERAL REPUBLIC OF GERMANY, AUSTRALIA AND EVEN THAILAND.

OUR GOAL IS TO PROVIDE A FORUM TO BRING TOGETHER THE ENTIRE SPECTRUM OF BIOTECHNOLOGY FIRMS FROM THE LARGEST TO THE SMALLEST, TO WORK ON AREAS OF COMMON INTEREST AND CONCERN. (For the record, we do not consider our association a competitor of IBA but rather complimentary to its efforts -- with the Industrial Biotechnology Association representing the unique interests of the larger, well established companies -- and the ABC providing a forum for companies of all sizes to meet and work together.) Approximately 10% of our biotechnology firms are also members of IBA.

AS FOR MYSELF AND MY PERSPECTIVE, I HAVE APPROXIMATELY 20 YEARS EXPERIENCE IN THE AREA OF INDUSTRIAL BUSINESS DEVELOPMENT.

I have been a line manager of a small aerospace testing firm which we successfully converted into a pollution testing laboratory in order to survive the completion of the Apollo Program. I HAVE SERVED ON THE CORPORATE STAFF OF SEVERAL FORTUNE 500 COMPANIES IN NEW PRODUCT, NEW VENTURE, CORPORATE DEVELOPMENT AND MERGER AND ACQUISITION CAPACITIES. AS HEAD OF MY OWN CONSULTING FIRM, I HAVE WORKED WITH THE MANAGEMENT OF HIGH TECHNOLOGY FIRMS IN THE COMPUTER, HEALTHCARE AND MOST RECENTLY BIOTECHNOLOGY INDUSTRIES -- primarily in the area of market analysis, competition strategy and corporate finance. AN

IMPORTANT OUTCOME OF THIS WORK WAS THE DECISIONS CONCERNING WHICH PRODUCTS TO DEVELOP AND COMMERCIALIZE. I HAVE ALSO WORKED WITH MAJOR U.S. AND FOREIGN FIRMS, UNDERWRITERS AND VENTURE CAPITALISTS IN THE EVALUATION OF HIGH TECHNOLOGY FIRMS FOR ACQUISITION OR INVESTMENT. AS YOU ARE AWARE, I AM CURRENTLY SERVING AS THE MANAGING DIRECTOR OF THE ASSOCIATION OF BIOTECHNOLOGY COMPANIES.

II

MOVING ON TO THE ISSUE BIOTECHNOLOGY WILL PLAY IN THE WORLD ECONOMY, I WOULD LIKE TO MAKE JUST TWO OBSERVATIONS.

1. FIRST, WE ARE STILL VERY EARLY IN THE DEVELOPMENT OF THIS TECHNOLOGY. JUST AS NO ONE WAS ABLE IN 1905 TO FORECAST THE MAJOR SOCIETAL IMPACT OF THE "HIGH TECHNOLOGY" AUTOMOBILE INDUSTRY (THE CREATION OF THE SUBURBS, SHOPPING MALLS, DRIVE THROUGH WINDOWS IN BANKS AND FAST FOOD, AND THE INTERSTATE HIGHWAY PROGRAM). I personally don't believe we have a good handle yet on the future societal impact of biotechnology.

   No one has a good handle, either, much less accurate statistics, on the current size of the industry. ABC is currently involved in a major study, in conjunction with a national accounting firm to develop detailed statistics on the industry. Early indications from that study are that the prior lack of knowledge about the activities of larger companies has caused us to seriously underestimate the size and near-term potential of the industry, while our lack of knowledge about smaller companies has caused us to underestimate the full breadth and potential impact of industry activities. Based on our current schedule, we plan to make the report on the results of this survey available to Congress, the industry and the press in early 1986.

2. A SECOND OBSERVATION on the eventual role of biotechnology IS THAT THE RAPID ACCEPTANCE OF BIOTECHNOLOGY IS AS MUCH A RESULT OF OUR NATIONAL SOCIAL CONCERNS AS IT IS A RESULT OF SCIENTIFIC BREAKTHROUGHS. THE CONCERN FOR ECOLOGY, THE CONCEPT OF "SPACE SHIP EARTH", THE INTEREST IN RENEWABLE RESOURCES AND RECYCLING HAS LED OUR SOCIETY TO A SHIFT FROM AN EMPHASIS ON CHEMISTRY TO AN INTEREST -- AND INDEED OPENNESS TO -- BIOTECHNOLOGY. Over the next few decades, I personally believe the benefits to society, from the more energy efficient production of speciality and individual chemicals based upon biotechnology processes, will have an even greater impact upon society than even the more spectacular application of biotechnology to health care. For example, looking back from the decades ahead upon 1985, I believe we will find that the development of Genentech's new fermentation process for producing Vitamin C (a $440 million market) will have a greater impact upon society at large than Genentech's development of either human insulin or human growth hormone.

III

MOVING ALONG TO ITEM 3, "HOW DO COMPANIES SELECT NEW PRODUCTS?"

BASED UPON MY 20 YEARS EXPERIENCE WORKING WITH LARGE AND SMALL COMPANIES, IN AREAS AS TRADITIONAL AND CONSERVATIVE AS THE FOOD PROCESSING INDUSTRY AND AS FAST MOVING AS THE SEMI-CONDUCTOR, COMPUTER SOFTWARE, HEALTHCARE AND MOST RECENTLY BIOTECHNOLOGY INDUSTRIES, I HAVE FOUND A BASIC CONSISTENCY IN HOW COMPANIES SELECT NEW PRODUCTS. SOMEWHAT OVERSIMPLIFYING THERE ARE THREE FACTORS:

1. **MARKET SIZE** - COMPANIES GENERALLY WANT PRODUCTS THAT CAN INFLUENCE THEIR SALES BY 1% TO 10% (I.E. THEIR SHARE OF THE TOTAL MARKET WILL BE EQUAL TO 1% TO 10% OF THEIR CURRENT SALES). There are exceptions of course. For example, those companies highly dependent on a single product -- the pharmaceutical companies and super-computer companies come to mind -- a bigger hit is required to survive and grow. Multi-divisional corporations, will accept products proposed by operating divisions that are only 1% to 10% of divisional sales. THE IMPLICATION FOR THE BIOTECHNOLOGY INDUSTRY THAT IN ORDER TO ENCOURAGE THE COMMERCIALIZATION OF THE ENTIRE SPECTRUM OF OPPORTUNITIES IN BIOTECHNOLOGY YOU WILL WANT TO ENCOURAGE A FULL SPECTRUM OF DIFFERENT SIZE COMPANIES.

2. **PROPRIETARY POSITION** - Companies are not generally interested in products in which they must bear the cost and

risk of developing the market while a competitor, who has not had similar costs, can simply jump on the bandwagon *if* the product proves to be successful and *when* the market has been established.

Now DEPENDING ON THE MARKET, THERE ARE A WIDE RANGE OF METHODS TO GAIN A PROPRIETARY POSITION. FOR A SHORT LIVED PRODUCT, SUCH AS A PET ROCK, SIMPLY BEING THERE FIRST IS SUFFICIENT TO ESTABLISH A PROPRIETARY POSITION. BY THE TIME A COMPETITOR CAN TOOL UP, THE MARKET IS GONE. For others, such as consumer products, a strong brand name and an aggressive sales force is usually sufficient to establish and maintain a proprietary product position. THE COMPUTER INDUSTRY HAS BEEN VERY EFFECTIVE IN USING HIGH INITIAL PRICES TO RECOVER DEVELOPMENT COSTS AND THEN DROPPING PRICES RAPIDLY TO DISCOURAGE THE ENTRY OF COMPETITION. THERE ARE ALSO THE MORE TRADITIONAL COMPETITIVE POSITIONS BASED UPON PATENTS AND TRADE SECRETS AND WHAT IS REFERRED TO IN SOME INDUSTRIES AS THE "REGULATORY PATENT" - LEAD TIME YOU HAVE OVER A COMPETITOR WHO MUST STILL UNDERGO A LENGTHY REGULATORY APPROVAL PROCESS.

There is currently a good deal of thought being given on the part of biotechnology companies on how to establish the strongest proprietary position for their new products. The hesitency of some of the larger companies to even admit they are working in biotechnology is a manifestation of this concern about maximizing their proprietary position

3. **FUNDING** - THE THIRD MAJOR FACTOR IN SELECTING A PRODUCT TO BE DEVELOPED IS THE AVAILABILITY OF ADEQUATE FUNDING TO BRING THE PRODUCT TO MARKET. IN THE INTEREST OF TIME, I WOULD MAKE JUST TWO COMMENTS:

(A) THE CURRENT STATE OF THE DEVELOPMENT OF COMMERCIAL BIOTECHNOLOGY IS VERY MUCH INFLUENCED BY THE AVAILABILITY OF VENTURE CAPITAL AND PUBLIC MARKET FINANCING. BECAUSE OF THE EASE OF "GOING PUBLIC" WITH A HEALTH CARE PRODUCT IN THE EARLY 80S, THE NEWER BIOTECHNOLOGY COMPANIES ARE HEAVILY ORIENTED TOWARDS THE HEALTHCARE INDUSTRY. As I alluded earlier, many of the potentially important applications of biotechnology, such as pollution control and toxic waste treatment, have not yet received venture capital funding.

Of course, some of those products will eventually be developed by the larger established firms if the products are perceived to meet market size, proprietary position, and potential financial return criteria to justify the funding investment.

(B) REGULATION ENTERS THE NEW PRODUCT DECISION PRIMARILY AS A COST FACTOR -- BOTH AS A COST OF OBTAINING REGULATORY APPROVAL AND THE COST OF RUNNING THE COMPANY/PROJECT (SALARY, RENT, ETC.) UNTIL REGULATORY APPROVAL IS OBTAINED. For example, a new biotechnology company will not enter into the development of a human pharmaceutical product unless it has developed a detailed strategy, including such sources of funding as additional equity and limited R&D partnerships, to cover the costs of obtaining regulatory approval and operating during the period of anticipated or unanticipated regulatory delay.

IV

THE FOURTH ISSUE IS ON GOVERNMENT POLICY THAT WILL HELP THE BIOTECHNOLOGY INDUSTRY TO PURSUE A GREATER SCOPE OF PRODUCT DEVELOPMENT. I WILL JUST LIST FIVE ISSUES. A MORE DETAILED DISCUSSION IS CONTAINED IN MY WRITTEN TESTIMONY.

1. BASIC RESEARCH - SCIENTIFIC BREAKTHROUGHS DO NOT APPEAR IN A VACUUM BUT RATHER ARE BASED UPON A LARGE NUMBER OF SMALL ADVANCES, MOST OF WHICH HAVE COME FROM BASIC RESEARCH FUNDING. BIOTECHNOLOGY REPRESENTS THE RESEARCH FUNDING INVESTMENTS MADE THROUGH THE NIH AND NSF GRANTS OF THE 1950S AND 1960S. WITHOUT CONTINUED GOVERNMENTAL RESEARCH FUNDING NEW BREAKTHROUGHS WILL BE MUCH LONGER COMING.

2. Education of Bioprocessing Engineers - The ability to turn these laboratory achievements into commercially viable ventures will be based upon the ability of this country to educate an adequate number of bioprocessing engineers. The training of these engineers is beginning to be undertaken by a number of educational

institutions. However, without additional emphasis on this area of education, we will soon be talking about a bioengineering gap.

3. SMALL BUSINESS INNOVATIVE RESEARCH (SBIR) GRANT - The concept is excellent. However, as currently administered it creates severe problems for the small innovative company -- namely, what is a small company supposed to do with its staff for the six to twelve month gap between Phase I and Phase II funding. Companies seek a continuous flow of funding to maintain employees as well as the research momentum. A MECHANISM MUST BE FOUND TO CONTINUE PHASE I FUNDING DURING THE SUBMISSION AND REVIEW PERIOD FOR PHASE II FUNDING.

4. PRODUCT LIABILITY - Without product liability, the biotechnology company is not only worried about its survival in the event of a lawsuit, but it can't enter into clinical trials with medical institutions that require the producer to cover the risk of product problems.

MANY BIOTECHNOLOGY COMPANIES ARE UNABLE TO OBTAIN COVERAGE OR AFFORD THE PREMIUMS IF THEY CAN OBTAIN COVERAGE, The short-fall between insurance demand and coverage is $7 billion today; in 1987 it will be $47 billion. This insurance crisis is expected to continue.

5. INTERNATIONAL TRADE - BIOTECHNOLOGY IS AN INTERNATIONAL BUSINESS. THE UNPREDICTABILITY OF EXPORT CONTROLS MAKES MANY POTENTIAL OVERSEAS PARTNERS WONDER,

SHOULD WE JOINT VENTURE WITH A U.S. COMPANY OR WITH OTHER DEVELOPED COUNTRIES WHOSE TRADE POLICY IS MORE PREDICTABLE?"

To prevent U.S. developed biotechnology and jobs from moving overseas, U.S. biotechnology companies must have access to foreign markets. For example, West Germany has approved interferon for therapeutic uses, but FDA laws bar/prevent U.S. biotechnology companies from exporting to this legitimate market. Biotechnology companies, who have high burn rates for capital investments into product development, must have access to legitimate markets.

THE ASSOCIATION OF BIOTECHNOLOGY COMPANIES BELIEVES THAT READY AND PREDICTABLE ACCESS TO LEGITIMATE FOREIGN MARKETS FOR BIOTECHNOLOGY RAW MATERIALS, IN-PROCESS COMPONENTS AND PRODUCTS IS KEY TO THE INDUSTRY'S CONTINUED GROWTH. WE HAVE PREVIOUSLY DISCUSSED THIS ISSUE WITH SUBCOMMITTEE MEMBERS AND THEIR STAFFS TO DISCUSS THE IMPORTANCE OF THE PHARMACEUTICAL EXPORT AMENDMENTS OF 1985 TO THE BIOTECHNOLOGY INDUSTRY.

* * *

MR. CHAIRMAN AND MEMBERS OF THE SUBCOMMITTEE, I THANK YOU FOR THE OPPORTUNITY TO SPEAK TO YOU THIS MORNING. I WOULD OF COURSE BE HAPPY TO ATTEMPT TO ANSWER ANY QUESTIONS YOU MIGHT HAVE.

Mr. **Wyden**. Thank you for your statement very much, Mr. Hyer. Dr. Blumenthal.

TESTIMONY OF DAVID BLUMENTHAL

Mr. **Blumenthal**. Thank you, Mr. Chairman, and members of the subcommittee. Thank you for affording me the opportunity to appear before you today. The purpose of my remarks is to discuss the extent and implications of industrial support of university research in the field the OTA has called the new biotechnology. In particular, I would like to address three questions that are of particular interest to industries, universities, and Government.

These questions are: How important is university research in biotechnology? What are the benefits and research to involved universities and industries and what are some of the implications for Federal policy of the growing industrial support of university support in this vital area of investment? In addressing these questions, I will be relying primarily on a survey that we conducted in the spring of 1984 of managers in a randomly selected sample of 106 U.S. biotechnology companies. There are, however, some other studies which I will occasionally refer to in delivering my remarks. Before proceeding, let me just cite for the record that our study is not entirely complete and some of our findings may be subject to change as we finalize our analysis later on.

How widespread are university/industry relationships in the field of biotechnology? I think the answer has to be very widespread. Nearly one-half of biotechnology companies in the United States say that they support some research in universities in the field of biotechnology. More than 90 percent of all universities say that they receive at least some industrial support of research in the life sciences.

We estimate that industry in 1984 provided universities about $120 million to do research in the area of biotechnology and that this constituted about one-fifth of all the research funds that were available for universities to do research in this field. Note that in the average scientific field industry fund s are about 5 percent of all research.

What are some of the benefits to universities, industries, and society from this kind of support of university research? I think there are benefits probably to all parties. For companies, there are the opportunities to educate and train their own staff, the opportunities to recruit very talented young scientists and faculty, and for smaller companies, especially, there is the opportunity to enhance the prestige of their companies and thereby to gain investors in their companies through association with powerful and outstanding academic institutions.

Perhaps most striking, however, when talking about the benefits to companies from this kind of research, is the role that university industry research relationships seem to be playing in the development of commercially useful products and processes. Companies supporting university research report that 17 to 23 percent of all the biotechnology patent applications that they have filed over the last 5 years have resulted from their investments in university research.

What are some of the benefits for universities? Well, there is first of all the direct financial support of research in a very dynamic and important area of investigation. There is also the potential income that is generated from patents developed with industrial support of research and owned by universities. And there is finally the opportunity to exchange information with scientists and to gain the kind of intellectual and educational stimulation that results from that interaction.

There are also, however, I think, clear risks to universities from these associations with industries, and we can provide documentation for that as well. One risk concerns the free and open communication of information.

Forty percent of companies that we surveyed report that at least one trade secret has resulted from the research that they have supported in universities. Faculty with industry support in the area of biotechnology are four times as likely as faculty without industry support to report that they have developed a trade secret based upon their university research.

As you know, trade secrets cannot be published or shared with colleagues or students who are not directly involved in the project that developed that research or aren't working in other capacities for the company involved in it.

Second, industrial support may tend to shift university research from more basic investigation toward more applied investigation. Seventy-two percent of companies report that the typical length of their agreements with universities is 2 years or less and actually about half of the companies report relationships are less than or equal to 1 year in duration.

The NIH, in 93 percent of its grants, provides money for at least 3 years. Obviously agreements that tend to be of very short duration are likely to be much more applied in nature.

The challenge, Mr. Chairman, at this point is to craft methods which preserve the benefits of university/industry relationships while reducing the risks. The Federal Government has a role in this effort.

First, the Federal Government may be able to reduce the tendency of researchers who work with biotechnology companies to keep their research results secret. I think you can do this by crafting improved methods for protecting the intellectual property of faculty and companies while also permitting its disclosure.

Second, the Federal Government can play an important role in helping universities and individual researchers to negotiate agreements that avoid conditions and restrictions that universities may find difficult to live with. The Federal Government can do this by continuing its strong support of research and training in the field of biotechnology. The availability of a secure and steady option to industrial funding of research, it seems to me, will strengthen the negotiating position and the resolve of universities to enter agreements that they feel comfortable with. This kind of support will insure they will enter those agreements because they offer the most exciting and challenging opportunities for them to develop their ideas because they feel their labs may close down or if they fail to get that funding.

It also seems to me that providing our Nation's biotechnology researchers in the universities with the best possible way to exploit their skills is vital to future progress in this essential field. Thank you very much.

[The prepared statement of Mr. Blumenthal follows:]

TESTIMONY OF DAVID BLUMENTHAL, M.D. BEFORE THE COMMITTEE ON ENERGY AND COMMERCE, U.S. HOUSE OF REPRESENTATIVES

Mr. Chairman, members of the the Committee, thank you very much for affording me the opportunity to appear before you today. My name is David Blumenthal. I am executive director of the Center for Health Policy and Management of Harvard University's John F. Kennedy School of Government and a practicing internist at the Massachusetts General Hospital in Boston, Mass. The purpose of my remarks today is to discuss the extent and policy implications of the industrial support of university research in a field that is vital to our nation's health and economic prosperity — the field of biotechnology.

For the last three years, together with colleagues at Harvard and the University of Massachusetts, I have been studying the varying relationships which have developed in recent years between universities and industries in this country. Our investigation has focussed particularly on relationships in which companies support universities to conduct research involving certain revolutionary biological techniques that the Office of Technology Assessment has called the "new biotechnologies."

The new biotechnologies have grown increasingly familiar to the lay public because of their extensive coverage in the media. Perhaps the most widely known of these techniques is recombinant DNA technology, also known as gene splicing, genetic engineering or gene cloning. Recombinant DNA technology has been used to produce such agents as human insulin, human growth hormone, interferon and interleukin-2, whose promise as an anti-cancer agent was so widely reported just two weeks ago. Other research techniques included in our definition of biotechnology are hybridoma or monoclonal antibody technology, gene sequencing, gene synthesis and several others.

In my remarks today, I would like to briefly address three basic questions of wide interest to industries, universities and government:

1. How extensive is industrial support of university research in biotechnology?
2. What are the benefits and risks to involved universities and industries?
3. What are the implications for federal policy of the growth of university-industry research relationships?

In addressing these questions, I will be relying for the most part on a survey we conducted during the Spring, 1984 of managers in a random sample of 106 U.S. biotechnology companies. I will occassionally supplement data from that survey with preliminary findings from two other studies we have done: a survey of administrators in nearly 100 universities and medical schools; and a survey of nearly 1300 faculty in the life and physical sciences within a subset of those universities.

Before proceeding, let me state for the record that our study is not complete and that some of our findings may be subject to change as we complete and refine our analysis.

How widespread are university-industry research relationships in biotechnology? The answer is: very widespread. Nearly one half of companies who support or conduct research in biotechnology fund some biotechnology research in universities. More than 90 percent of universities in our sample received some industry research funds in the life sciences.

We estimate that industry provided universities approximately $120 million in biotechnology research support during 1984. According to our calculations, this constituted about one fifth of all the funds available to universities for biotechnology research that year. Note that in the average scientific field, industry funds only about 5 percent of university research. I think it is fair to say that a high level of mutual dependency has developed between universities and industry in the field of biotechnology.

Our research shows that university-industry research relationships have real benefits for universities and for industries, and probably for society as well. For companies, the benefits include the education and training of company staff, the opportunity to recruit talented young scientists, and especially for small companies, a chance to enhance their firm's prestige through association with outstanding academic institutions and investigators. This, in turn, helps small companies to attract investors.

Perhaps most striking, however, is the role that university-industry research relationships seem to be playing in developing commercially useful products and processes. Companies supporting university research report that 17 to 23 percent of all the biotechnology patent applications they have filed over the last five years have resulted from their university investments. What is more, per dollar invested, university research seems to be generating 2 to 4 times as many patent applications as research supported in other sites. This last finding is subject to certain technical limitations. Nevertheless, it seems fair to say that university-industry relationships in this field seem to be playing an important role in moving knowledge from the bench to the bedside and the production line.

What are the benefits for universities? First, there is the direct financial support provided for research in a dynamic field of science. Second, there is the potential income from licenses on patents developed with industry support but owned by universities. Third, there may be educational and scholarly benefits resulting from contact between students and faculty on the one hand, and industrial scientists and industrial concerns on the other. We are in the process of investigating both the extent of patent income that may result from university-industry relationships in biotechnology and their effect on faculty productivity and the educational experience of students. We hope to be able to share our results on these matters with the Committee at a future time.

Our documentation of the benefits of industrial support of university research will undoubtedly come as welcome news to those universities and industries who are not already aware of these dividends. Less welcome, perhaps, will be our documentation of the risks these relationships pose for traditional university values and practices, such as the free and open communication of information.

First, evidence from several of our surveys indicates that university-industry research relationships do increase the level of secrecy among faculty. Forty percent of companies report that at least one trade secret has developed out of their university research. Biotechnology faculty with industry support are four times as likely as faculty without such funds to say that their work has produced a trade secret. By definition, research results treated as trade secrets cannot be published or shared with colleagues or students not directly involved in the project.

Second, industrial support may tend to shift university research toward more applied projects. Seventy-two percent of companies report that the typical length of their aggreements with universities is less than two years. In contrast, 93 percent of NIH grants last at least three years. Projects of relatively short duration are likely to be more applied in nature. Undoubtedly, some university-industry research arrangements, especially the large, highly publicized, long-term relationships, do support research that is fundamental in nature. However, our findings suggest these research agreements are not typical of all existing arrangements.

Third, in certain instances, university-industry research relationships that include support for graduate students may pose certain risks for their education. About one-third of firms that support the training of graduate students in the life sciences impose some conditions on the research of those students. Most commonly, these firms require students to work on projects defined by the industry sponsor. While this may seem a reasonable request on the part of industry, no comparable condition is imposed for most federal training support. Further investigation is needed to see how, if at all, conditions imposed by industrial sponsors affect the educational experience of involved students.

It is premature at this point for us to advance final or simple conclusions about whether university-industry research relationships are on balance beneficial for universities, industries or society at large. And regardless of what we conclude, universities and industries in a free society should have wide latitude to develop such relationships. The challenge for all interested parties is to craft methods which preserve the benefits of these relationships while reducing the risks. In this effort, the federal government has a role, especially in reducing the risks to universities.

First, the federal government may be able to reduce the tendency of biotechnology researchers and companies to keep research results secret in order to protect their proprietary value. There seems to be growing concern among some industrial patrons of university research that patent law may be inadequate to protect intellectual property in biotechnology, as well as certain other fields. If this proves to be the case, the use of secrecy to safeguard biotechnology research results in the university and elsewhere may grow. By designing legal mechanisms that allow researchers both to protect and to disclose their intellectual property, the federal government could contribute importantly to open communication of biotechnology research results on the nation's campuses now and in the future.

Secondly, the federal government can play an important role in helping universities and individual researchers to negotiate agreements that avoid conditions and restrictions that universities find objectionable. The federal government can do this by continuing its strong support of research and training in biotechnology.

Such support would be in the national interest in any case. Our figures clearly show that despite its higher than average investment in biotechnology, industry shows no prospect of supplanting federal research funds in this field and would be unlikely to match any substantial federal cutbacks in research support.

However, an additional benefit of continued federal support of biotechnology research and training in academic institutions is that such support provides the nation's most talented academic researchers with a steady, secure option to industrial funding of their research. If those investigators still seek industrial support, and I am convinced that many will continue to do so, they will enter those relationships freely and confidently, secure in the knowledge that they can negotiate agreements that protect basic university values without fearing that losing industrial support will jeopardize their ability to continue their research.

Since the great majority of companies deeply respect our nation's academic institutions and the values they uphold, strengthening the resolve of universities to bargain for what they hold dear should not jeopardize university-industry partnerships over the long-term. Continued federal support can, however, make certain that investigators enter these relationships because of the challenge and opportunity they offer, because they represent the best possible use of their valuable skills. Permitting our nation's investigators to use those skills in the best possible way is vital to progress in biotechnology and to realizing its immense potential benefits for improving our people's health and economic well-being.

Mr. **Wyden**. Well, thank you very much and all our panel members for excellent presentations. I recognize the gentleman from Minnesota for questions. Does my colleague from Ohio or my colleague from Virginia, would they like to make an opening statement?

Mr. **Luken**. I have no opening statement.

Mr. **Wyden**. Gentleman from Virginia.

Mr. **Bliley**. Mr. Chairman, thank you. I want to commend the chair for conducting this series of hearings and for the concern he has shown to assess the current state of development of the biotechnology industry and the efforts to adequately regulate it. It is certain the application of biotechnology has the potential to significantly improve the lives of people all over the world by advances in areas such as drug development, food production, and waste disposal. Limits of the application of this new technology are defined only by the imaginations of human beings.

Government has an important role to play in the development of biotechnology, and I again commend the chair for his recognition of the importance of that role. Government-sponsored and funded basic research has laid the foundation for some of the newest and most exciting methods of biotechnology. These efforts must not diminish as these new methods are used commercially. As commercial development begins, however, Government must assume new roles, both in support of the commercial application of the new technology and as a regulator of it to ensure that public health and safety are not endangered by its commercial application.

We have before us distinguished witnesses from industry academia, and Government. I am looking forward to hearing from these witnesses the current status of the biotechnology industry, the efforts that have been undertaken to promote and adequately regulate it; and recommendations as to how all concerned can proceed together to fulfill the promise of this new technology.

Mr. **Wyden**. Without objection, so ordered. The gentleman from Minnesota.

Mr. **Sikorski**. I thank the gentleman. I just have two questions for Dr. Blumenthal. One is on the issue of trade secrets and commercial product development. I think it is fair to say that the research undertaken at universities in this country is based on basic research that was Government funded; is that correct?

Mr. **Blumenthal**. In the great majority of cases, that is correct.

Mr. **Sikorski**. There is a lot of funding, further government funding that takes it beyond the basic research stage as well. My concern is with some newspaper articles over the last several months dealing with foreign companies arranging relationships with various universities and their hospitals or other facilities that utilize this U.S. taxpayer-financed research for the development of commercial products that then end up as the intellectual or property right of this foreign company.

Do you see a lot of this? Is this a problem or is my concern falsely positioned?

Mr. **Blumenthal**. Let me say, to begin with, that the data we collected was from biotechnology companies with offices in the United States, and we didn't ask them to identify whether they were foreign or domestic. Sometimes it is not obvious from where the office is located what the ownership is. There are multiple and complex relationships, on which I am far less expert than the gentleman on my left, between United States biotechnology companies and foreign companies.

I do think it is a risk that is run when you allow foreign companies to fund substantial amounts of university research. There are clearly cases where foreign companies do so. In my own hometown of Boston, the Hoechst Co. is funding a large amount of research at the Massachusetts General Hospital. I have heard this subject discussed many times and it is obvious that there is also a two-way flow of information, that companies from abroad bring their trade secrets with them and educate American researchers in those trade secrets in the process of doing cooperative research.

I don't feel at this point that I have enough information to say to you whether on balance the flow in and the flow out are equal or more in one direction or another. I do think it is a more complex topic than a simplified model of foreign companies coming in and taking basic American progress in research away. I do think they also obviously bring money that promotes progress, and they also bring some know-how.

Mr. **Sikorski**. My last question is, in your paper entitled Industrial "Support of University Research in Biotechnology," you recommend to university administrators they may want to devote more of their limited resources to monitoring relationships with smaller companies than with large ones. What would you suggest university administrators look for, guard against, and why?

Mr. **Blumenthal**. Let me put that in context. That is from an article which I shared with the subcommittee. We found that the types of situations that universities identify as potential problems are more prevalent in relationships with small companies than in relationship with large companies, and these, for example, include situations in which researchers own equity in a small company and receive research funding to do university research from that company.

Also trade secrets are much more commonly reported in relationships with small companies than with large companies. That seems to me to indicate to universities that if they are concerned about these situations, and if they have policies regarding these situations, that they ought to look more closely at the contracts that exist with small companies.

It doesn't by any means mean they should not get into those relationships, because I think that they are very productive in many ways. It does mean, however, if they have one person doing that kind of monitoring and he has to decide whether to monitor the large company closely or the small company closely, that he probably should look on the relations with the small company.

Mr. **Wyden**. The chair thanks the gentleman.

The gentleman from Ohio.

Mr. **Luken**. Thank you, Mr. Chairman.

I have only been here for part of it, and I am going to be relieved of the responsibility of any extensive examination because we have to go vote, but, Dr. Blumenthal, you mention that the issue of designing legal mechanisms that allow researchers both to protect and disclose their intellectual property, and in this regard the Federal Government could contribute importantly to open communication of biotechnology research results on the Nation's campuses now and in the future. Is this happening? Is the Federal Government contributing to this communication?

Mr. BLUMENTHAL. I think that patent law is an important device that permits researchers to claim intellectual property rights to a research funding and also to disclose and publish that information. That seems to me a preferable way of retaining intellectual property rights than keeping the results of research secret.

Patent law is, of course, Federal law, and I have heard concern expressed—and perhaps representatives of the industry can comment on this in a more informed fashion—I have heard concern expressed that in the field of biotechnology patent law has not kept up with the progress of technology, that it is unsuited to protecting intellectual property rights in this very dynamic field and that it may be necessary, as in the case of software and other similar areas, to modify the law or find some better device for protecting intellectual property.

Mr. LUKEN. Aren't we pursuing it? Is our Judiciary Committee holding hearings and framing legislation, Mr. Hyer, or, Dr. Blumenthal? Do you think it is moving along?

Mr. BLUMENTHAL. I can only tell you the industry representatives that I have talked to about this continue to express concern about it. I really can't give you an informed comment on any progress in committees of Congress on this issue.

Mr. LUKEN. There is no legislation. Rather the legislation is not keeping pace. Is that your impression, Mr. Hyer?

Mr. HYER. I don't have very much knowledge of that issue.

Mr. LUKEN. You are aware of the issue?

Mr. HYER. Yes.

Mr. LUKEN. Then it is a concern obviously. You agree that it is a concern that patent laws, that the legislation in this area is not keeping up with the science?

Mr. GOLDHAMMER. I think the major problem that has been expressed by our membership is the Patent Office hasn't had enough examiners to deal with the tremendous number of patent applications. There were some questions about the patent law, in particular whether novel plants created by genetic engineering could be patented. That has been resolved, I think, 2 months ago by a court decision in favor of their patentability under the General Patent Act.

As to the main issues here, it has been up to date a question of the Patent Office being able to keep up with the number of applications, and in this country applications have lagged 2, 2½ years until a patent has been issued, which is far different from situations over in Europe and Japan.

Mr. LUKEN. As you see it, it is not a lack of legislation but a lack of personnel swamped by the applications from this new area or newer area?

Mr. GOLDHAMMER. That is what it has been. We have held discussions with the people over at the Patent and Trademark Office on this subject and have tried to contribute as much of our resources to educating the examiners to get them up to speed.

Mr. **Luken**. Can I just pursue one thing a little more, in the area of Dr. Blumenthal and the other gentlemen also, the Federal cutbacks you have mentioned, obviously they loom large in any area of research or any area where the Federal Government has been involved. Do you feel this is the major problem as far as you are concerned, the potential loss of Federal funding for research? You have indicated in your testimony that you don't believe that industry can supplant the Federal research grants.

Mr. **Blumenthal**. No, I don't think there is much dispute about that. Industry, even at the 20-percent figure we talked about, doesn't come close to matching other sources of support, notably the Federal Government, and major cutbacks in Federal support would inevitably reduce the total amount of research done in universities and also shift it toward, in more applied directions.

Mr. **Luken**. This is one area where it graphically demonstrates what may happen under our Gramm-Rudman legislation, because I don't believe there is any protection for research grants of this kind. So it would bear the full brunt of those draconian cuts. It is something for us to consider.

Thank you, Mr. Chairman.

Mr. **Wyden**. I thank the gentleman. He makes an excellent point certainly about Gramm-Rudman. We will, first of all, ask all of our panel members to accept some questions in writing just in the interest of time. I think that is going to be necessary.

And I just have a couple of very quick questions for you, Mr. Goldhammer, particularly, with respect to your comments about applications of biotechnology beyond health care. I think you told the subcommittee you have seen investments in new plant varieties and pesticides and frost damage control, pollution control. We would be very interested in knowing in the area of plants to what extent is the work undertaken by your members a target increasing nutritional value of crops, as well as output of the American farmers?

Mr. **Goldhammer**. One of our member companies has done this. The patent decision I referred to on a new plant variety was a plant that specifically is of enhanced nutritional value. It is a corn plant which has—produces a greater amount of tryptophan, which is an essential amino acid for both humans and animals. And the hope is that advances in this direction will create more nutritional animal feeds, which, of course, is one step in the food chain, which will make it more economical to feed the animals and then eventually feed the humans. This is one specific example that has come to fruition.

I think there is a considerable amount of research looking into this area to create plant varieties of enhanced nutritional capabilities.

Mr. **Wyden**. Mr. Goldhammer, I thank you. I would be very interested in pursuing one or two other questions when we get back. We will suspend again just for a couple of minutes.

[Brief recess.]

Mr. **Wyden**. The subcommittee will come to order and we do appreciate the patience of our panel members. Just one additional question, if I might, for Mr. Hyer and Mr. Goldhammer.

Gentlemen, are there disincentives to commercial investment in improving the of performance micro-organisms to degrade pollutants?

The subcommittee is very interested in that. If you believe that there are and could tell us, that would be very helpful.

Mr. **Goldhammer**. I think that the questions, as I pointed out in my statement, are more of an uncertainty about regulatory policy right now and possibly legal questions. I think certainly, as the staff is aware, the one example that we have had which has been approved of EPA releasing a genetically engineered macro-organism into the environment is under litigation and it is conceivable applications for pollution control might also be subject to litigation.

EPA right now is still working through their policy and maybe Dr. Moore this afternoon will be able to elaborate on this, as to how they plan to look at this particular class of genetically engineered micro-organisms. So I wouldn't characterize it as a lack of interest from the commercial sector.

There are a number of companies out there that are actively working in this area, and as a result there are some applications which are currently being used in contained facilities for the degradation of specific pollutants.

It is possible those might be expanded to the environment once the regulatory uncertainties are clarified.

Mr. **Wyden**. Mr. Hyer, same question about commercial disincentives.

Mr. **Hyer**. I believe probably the strongest commercial disincentive is basically the question of the bias against genetically engineered bacteria. Bacteria have been used quite regularly and a number of companies are currently supplying various products for mineral collection for detoxification. These are products that have evolved through traditional biotechnology methods.

I think those companies which try to use a genetically engineered approach toward the microbes are going to be at a distinct regulatory disadvantage as opposed to those companies that use the more natural methods that are currently commercially available.

Mr. **Wyden**. Let me recognize our minority counsel at this point for any questions he may wish to pursue.

Mr. **Wilson**. Thank you, Mr. Chairman.

I have just a couple questions for Messrs. Hyer and Goldhammer.

Are there any current regulatory or legal restrictions that discourage your members from developing and marketing the orphan products that have been discussed this morning?

Mr. **Hyer**. I don't believe that there are regulatory restrictions. I think the major problems are strictly the economics. Most of the companies in the biotechnology industry tend to be very small companies, very much concerned about their own survival. I mean it is pretty well agreed that—if you take an average of the companies, most will not survive. They are going to have to pursue those activities which provide the greatest immediate or financial incentive or the ability to raise funding.

The products that are going to have a longer leadtime or have less certain markets, smaller companies can't afford to get to it at the present time, but again that is a competitive market situation, not a legislative one.

Mr. WILSON. Mr. Goldhammer.

Mr. GOLDHAMMER. The only area that I think there is a lack of research that probably could be eased somewhat is, say, in the tropical disease area. I think as the committee is aware, these diseases are not endemic to this country, but overseas, and there are regulatory questions there, in particular whether one could export a vaccine for malaria in advance of approval by our FDA, which currently would be prohibited.

We think that the legislation could be put into place to remedy that situation, but in terms of the overall incentives for commercial development here, I don't think so. I think the legislation governing orphan drugs that was passed a couple years ago provides incentive and certainly pharmaceutical companies have taken advantage of that and I think there is now products on the marketplace that would not have been formerly.

Mr. WILSON. My other question is whether any of you are familiar with the efforts to promote and regulate biotechnology in foreign countries and what impact those efforts may be having on the ability of U.S. domestic manufacturers to export?

Mr. GOLDHAMMER. There has been an effort to try to coordinate international regulatory policies through the Organization for Economic Cooperation and Development, which is a group of all the Westernized countries. They met, I believe, 1½ weeks or 2 weeks ago to finalize their recommendations. It is a nonbinding report, just simply offering some recommendations.

It has not—apparently has not—been cleared yet by the State Department for general dissemination. We are looking forward to that and we certainly believe that the international efforts such as this to harmonize regulations are useful.

The other area which certainly plays an important role here is individual country's regulatory policies in the health care area. Certainly the Japanese have very much a different regulatory situation than this country does, and Western Europe has a different one. That is the cost of doing business in the international marketplace.

Certainly one way to get around that is to license products or enter into joint ventures with foreign countries.

Mr. WILSON. I have no further questions.

Mr. WYDEN. Just a couple other questions if I might.

Mr. Hyer, in terms of your members and their view with respect to reliance on university researchers, do they see this as something that is temporary essentially until the industrial scientists learn the techniques, or is this more likely to be a more permanent way of doing things?

Mr. HYER. Given the wide diversity of our members, it is going to be very hard to speak for them in general, but I would say that we are right now still very much in a research stage and therefore very dependent on the university because we are doing a large number of different projects.

I think as we start honing in on particular products, which will have a large impact on the economy—I am thinking for instance of one of the major, I consider, breakthroughs which was announced several weeks ago with genetics' ability to produce vitamin C.

If you can produce a $440 million market with one strain of bacteria, you are interested now in industrial production, not in particular additional research and development.

Mr. **Wyden**. One other question, if I might, for you, Mr. Hyer. What is your understanding of the extent of commercial investment in improving yield and nutritional value of food crops for developing countries around the world?

Mr. **Hyer**. Again, given the companies which we work with, which tend to be the smaller companies, I am not aware of any major efforts of any of our members in that area.

Mr. **Wyden**. Mr. Goldhammer.

Mr. **Goldhammer**. This is a very, very early application of biotechnology. In the agricultural area, the scientific basis has lagged probably 10 years behind the scientific knowledge for, say, manipulating micro-organisms. Right now all that we are seeing is really test systems that people are working on in terms of genetic engineering, and I suspect it is really not going to be, for several more years, before we are able to develop the techniques for genetically engineering crop plants.

The systems that people are working on right now are things like petunias and tobacco, which are not likely to have commercial importance, but are simply a way of understanding how to move genes in and out of plants.

Mr. **Wyden**. Gentlemen, we thank you.

Just in the interest of time we are going to have to move along, but we are going to submit some additional questions to you in writing.

We thank you for your very helpful presentation and cooperation with the subcommittee.

Unless you gentlemen have further comments, we will excuse you.

Our next panel consists of: Robert Nicholas, Esq., Blum, Nash & Railsback, Washington, DC; Marc Lappé, Ph.D., fellow, Hastings Center, Hastings on Hudson, NY; and Dr. Richard Novick, director, the Public Health Research Institute of the city of New York, Inc.

If you gentlemen will come forward. We welcome all of you to the subcommittee today.

It has been a longstanding tradition of this subcommittee to swear all witnesses. All of you have the right to counsel, and the Chair observes the presence of the committee rules at the witness table throughout the presentation.

Do any of you who will be witnesses have any objection to being sworn this morning?

[Witnesses sworn.]

Mr. **Wyden**. We welcome you. We will make a copy of your prepared remarks part of the hearing record in their entirety. If you could summarize your principal concerns for the subcommittee in the interest of time, that would be most helpful.

Let us begin with you, if we might, Dr. Lappé.

TESTIMONY OF MARC LAPPÉ, FELLOW, HASTINGS CENTER, HASTINGS ON HUDSON; ROBERT B. NICHOLAS, PARTNER, BLUM, NASH & RAILSBACK, WASHINGTON, DC; AND RICHARD P. NOVIK, DIRECTOR, PUBLIC HEALTH RESEARCH INSTITUTE OF THE CITY OF NEW YORK, INC.

Mr. LAPPÉ. I have four principal concerns about the evolution of this industry. They deal with the problems of secrecy, problems of attention between private gain and public benefit, the issue of priorities, and the question of appropriate policies for regulating biotechnology.

Perhaps the best perspective on this emergent field is to note there has been a collapse between the normal distinctions between basic research and applied research. This graying of a distinction means a considerable volume of work that is being done in the private sector under the aegis of applied research is almost certainly generating information of fundamental basic value.

I am concerned that a considerable portion of this information may not be freely exchanged in the public sector, and that is one of the focuses of my concern today.

I am also concerned about the net benefits to society of this rapid explosion of the biotech industry. I believe that if the present trends in the concentration of biotech research in the private sector are encouraged, that the choices that this industry are likely to continue to make will probably downplay certain developments that are critical to the generation of public good.

Based on my discussions with biotech company leaders and my reading of the literature, the biotech industry's current priorities, in distinction with some of the previous testimony, appear to hinge considerably on the question of feasibility, high return on investment, short timeframe for product development, and indeed the existence of an available market; but, sometimes, that is a market that is created, generated, or manufactured by the companies whose products are being proferred.

This priority scheme is not likely to meet the social goals enumerated by international agencies such as the World Health Organization. These goals include reducing the impact of the major childhood killers, not just in tropical countries but in developed countries. These include, even in this country, bacterial dysenteries.

They also include increasing the protein yield of food crops. Controlling other major endemic diseases, particularly of livestock, is another critical goal.

The industry's product choices have tended to emphasize products with short-term development, with ready markets, so that ironically, instead of treating the livestock disorders carried by the tsetse fly, that limit production for a whole belt of countries in Africa, we have veterinary vaccines developed in the United States. Instead of vaccines for childhood killers, we have a product for treating hemophilia.

I would like to enumerate briefly a few other areas I think deserve more attention and encouragement. I think that there is a relative dearth of industry-sponsored products for converting biomass into useful energy sources. This is a need that we, as a nation have, and that the Third World countries have, as well.

That world, the developing world, is biomass rich and energy deficient. I believe the reason, in part, we haven't seen more of what I am deeming to be socially relevant choices is that this industry has been very substantially insulated from public opinion about its priorities. By focusing public debate on the largely antedated issue of biosafety or even the question of environmental hazard from intentional release of organisms, I believe that we have left this industry unfettered and free to choose its priorities and subsequent avenues of investment virtually devoid of public input.

Now, I would note that that might be an acceptable motif for an industry that was working in nonessential areas of development. But in the biotech industry, the products that are potentially made and the choices that are consequently made create opportunity costs. Manipulating DNA is not a skill that is universally distributed amongst a very large number of companies. Choices made by a company the size of Cetus may leave other choices unmade. The classic example is the choice Genentech made not to pursue a malaria vaccine while pursuing other avenues of short-term investments, such as developing a factor VIII for treating hemophilia or human growth hormone.

Like Professor Blumenthal, I am also concerned about the relationship between the acquisitions and sponsorships in this industry, because it restricts both the degrees of freedom that the research sector might elect and basic academic freedoms.

When multiplied many times over, the relationships that Professor Blumenthal described will have a reverberating effect on the entire academic sector. A real threat is that this emphasis on trade secrecy, and even the patent process, which allows information to remain latent and secret for a period while the patent is pending, means that there will be a privatization of knowledge. This knowledge is not just in the applied sector. This is some of the basic stuff that biology was evolving towards.

In the 1970's, the hope of the people who developed the recombinant DNA techniques was that this technique would unlock the secrets of the gene. Many of these secrets have remained secrets. We have what I term to be an exploitation of these genomes rather than an assembly of basic information available to all so we can move on a broad front in advancing this whole sphere of knowledge.

So, to sum up, I believe that almost the entire area of applied biotechnology research in the United States is unfortunately concentrated in the private sector, although most of the basic research is still publicly supported. This is quite different from the situation in Japan where there is a 50/50 partitioning of research that is supported by the private sector. From the outside looking in, this partitioning appears to create a de facto deferral of the government to the private sector in this country for setting priorities.

Now, if the record of the biotech industry's choices of their product developments to date is any measure of the future, this concentration of a policy choice in the private sector means inevitably that certain otherwise vitally important but initially unprofitable or risky ventures are not going to get undertaken. Such a situation, as I emphasized, has already occurred in the field of vaccines.

What I recommend, then, is a mechanism for both oversight and guidance for the biotech industry so that these important and often critical areas of development are at a minimum selectively encouraged. I think it is equally important a new mechanism to reduce dependence of the industry be put in place. Public members are needed on oversight committees. Congress should consider whether or not a regulatory body modeled after the public utility commissions would be appropriate, given the vital importance of this field.

Putting more public input into the priority decisions made about funding in this public sector would also augment the process of deprivatizing this vital industry and its information base. Coordinating this public input into policy recommendations of Congress would be geared ideally to encouraging selected areas of research that would assure that more applications would serve not just orphan drugs but drugs in the public interest.

Basic research, in fact, could be strengthened by offering further protections on intellectual property and, hence, freeing data and information that are now held as trade secrets by biotech companies. If carried out effectively, such strategies ideally would ensure project areas that serve the public good are also made economically viable and attractive, and if done equitably, I think these new programs and policies will appeal to those most likely to take the risk needed to assure full production; namely, those in the private sector who control the biotech industry itself.

[The prepared statement of Mr. Lappé follows:]

TESTIMONY BEFORE THE OVERSIGHT AND INVESTIGATIONS SUBCOMMITTEE

COMMITTEE ON ENERGY AND COMMERCE

US HOUSE OF REPRESENTATIVES

December 18, 1985

Marc Lappé, PhD

INTRODUCTION

No one now doubts that biotechnology has emerged as a powerful force in shaping the future of major areas of our economy. Developments in agriculture, energy production, and ecology promise to change the manner and degree to which scientists in developed countries control biological systems, and shape them to human ends.

Major ethical dilemmas are posed by the advent of these new capabilities. Choices made now about the first generation of products are likely to affect the long-term development and application of recombinant DNA technology. Who will be helped, who hurt, and who simply ignored is a critical issue of public policy. Congress plays the key role in shaping this public policy for both basic recombinant DNA technology research and its applications in the biotechnology industry itself.

My thesis is straightforward: If present trends in the concentration of biotechnology research in the private sector are encouraged or condoned, the choices of the biotechnology industry are likely to exclude or downplay certain developments critical to the generation of public good. By public good, I refer to creation of conditions of living and sustenance consonant with the greatest benefit for the greatest number of persons.

Based on my discussions with biotechnology company leaders and my reading of the literature, the biotechnology industrys' current priorities hinge on feasibility, high return on investment, short time-frame for product development, and the existence of a ready market.

This priority scheme and its variations has generated a first "crop" of biotechnology products that tend to downplay complex interactive products in favor of those that have singular applications. Such products include a broad range of medical devices and diagnostic reagents that augment the rapidity or sensitivity of existing diagnostic technologies; single-chemical herbicide resistance in certain high-yield plant varieties (notably the Nicotinia species that include tobacco); and improvements in the capabilities of the fermentation industry, particularly in brewing fermented products from grains.

Lacking is evidence for a concentrated policy for the long-term applications of biotechnology in areas like climate-specific crop selection, development of alternative energy sources, or integrated biomedical problem resolution. Where biotechnology has been "successful", it has generally been in the monodimensional product or genetically synthesized protein that has permitted the substitution of a purer product (eg, human insulin for porcine insulin) or the economic production of an otherwise expensive precursor (the amino acid phenylalanine in the prodcution of aspartame, the non-nutritive sweetner). What characterizes many of these first generation products is their immediate marketability (eg, the veterinary vaccines), their status as high "value-added" commodities, and concomitant high return on investment.

A similar public policy vacuum may explain the relative dearth of successful industry-sponsored projects for converting biomass into usable energy sources. One of the major sources of economic dependency of the developing world (and to a lesser extent, the developed one) is on the availability of inexpensive alternative energy supplies. The developing world is biomass rich and energy-deficient. Logical extensions of cellulose degrading systems for converting this rich biomass into usable energy could shift the existing imbalance and reliance of many countries on either oil cartels or developed countries as their primary sources of energy. The fact that heavy investment into these relatively feasible programs has not yet occurred suggests that factors other than international need drives the biotechnology industrys' choices.

I believe that the reason we have not seen more "socially relevant" choices is that this industry has been insultated from public opinion about its priorities. By focussing public debate on the largely antedated issue of biosafety or environmental hazard, the biotechnology industry has been able to chose its priorities and subsequent avenues of investment essentially free of government or public input.

Development decisions instead have been largely dictated by the basic economic realities of an industry that is heavily capitalized by individual venture investors and public offerings. These realities appear to demand early product development with high return on investment. Because of the concomitant trend towards acquisition of small biotechnology companies by large, multinational corporations, product choices by the acquired company are often dictated by pre-existing markets and products created by its new parent. A comparable analogy exists in the sponsorship of university research by large and small biotechnology firms.

In practice, these acquisitions and sponsorships restrict the degrees of freedom that the research sector might otherwise elect. Some of the choices are made to support the sponsoring organization, while others are less obviously constrained. For example, a research option ostensibly made under the umbrella of academic freedom may in fact be chosen because it complements a problem experienced by the sponsoring organization.

When multiplied several times over, such arrangements will have reverberating effects on the entire academic sector. A real threat is the resultant privatization of knolwedge that can occur when secrecy and patentability become dominant principles of academic research. The absence of sharing of knowledge by industry in contrast to academic researchers at major conferences is taken as an anecdotal, but sorry statement of the gulf between the two arenas of research.

Sometimes research decisions made in the public sector can drive the direction of a whole industry. A case in point would be research that led to the movement of resistance genes to the herbicide glyphosphate into crop plants. Since the patent for this herbicide is held by a single multinational company (Monsanto), increasing the number and variety of crop plants in which specific resistance can be conferred increases the likelihood of dependency on the herbicide by the farming community.

Since use of this expensive herbicide is likely to be most cost effective for the large conglomerate agricultural enterprises, it is not at all clear that such a development assists the small farmer here or in the Third World. For many of these individuals, success turns on developing crops that can be inter-tilled (with more than one species on a field); acquiring drought resistant varieties; or increasing the disease resistance of the seed stock. Such developments require considerably more genetic engineering than putting in a single gene for herbicide resistance, and promise greater, albeit much more long-term, returns on investment. With the notable exception of firms like Agrigenetics that has invested significantly in cassava root, an almost exlusively Third World crop, few companies have appeared willing to generate research strategems that would favor the labor-intensive, marginal farming characteristic of most of the world's needful areas.

SECRECY

The problem in agriculture is compounded by the sequestering and protection of germ plasm by the same multinational corporations that are engineering crops for specific attributes. The acquisition of virtually the entire seed-producing industry in the devloped world by major corporations reduces the public input into decision-making, specifically in areas of great public policy conern. Representative areas include ensuring an adequate base of genetic diversity in seed crops, and the availability of climate-specific varieties to small farmers. This concentration of plant genetic "wealth" in the private sector is symptomatic of a parallel problem in mammalian systems.

Because of the encouragement of the biotechnology industry to develop and maintain many of the genetic varieties of new recombinant organisms as trade secrets (See Roman Saliwanchik, Legal Protection for Microbiological and Genetic Engineering Inventions, Addison Wesley, 1982; pp 10 et seq), and the sequestering of actual gene sequences in privately held computer banks, the total amount of genetic knowledge being generated by the private sector is both unknown, and more urgently, unknowable and unusable by the public. This circumstance alone renders untenable the industry's position that continued unfettered and unrestricted private growth of biotechnology is in the public interest.

PRIVATE VERSUS PUBLIC SUPPORT

Almost the entire area of applied technology research in the United States is concentrated in the private sector, with most of the basic research still publicly supported. From the outside looking in, such a partitioning appears to create a de facto deferral of the government to the private sector for setting priorities.

If the record of the biotechnology indastry's choices of product development to date is any measure of their future performance, this concentration of power in the private sector means inevitably that certain otherwise vitally important but initially unprofitable or risky ventures do not get undertaken. Such a situation appeared to have occurred in the instance of the initial research into a malaria vaccine, although remarkably successful publicly supported research has now apparantly restimulated industry interest in this and other vaccines.

A POLICY DILEMMA

These initial observations and those developed more fully in my book, Broken Code (Sierra Club Books, 1985) suggest that there is a policy vacuum in biotechnology. What was initially a publically supported research base has now been almost entirely privatized. Government-sponsored or encouraged research, rather than increasing in porportion to the applied research funded by industry, has diminished in relative proportion. This tendency has meant that the actual policy choices of what ge[illegible] done has been largley deferred to the private sector.

If my analysis is correct, these choices have been largely self-serving, leaving whole sectors of potentially valuable research at best kept secret, or at worst, left undone. As I argue in Broken Code, this situation violates a basic moral code endorsed by the original organizers of the first recombinant DNA conferences (the Gordon and Asilomar meetings of 1975-6), namely that their work would be open to public scrutiny and would serve the public interest. Little if any public oversight and policy input now exists for the biotechnology sector. In some companies, Internal Institutional Biosafety Committees are carefully screened to exclude potential "activists"; Boards of Directors lack public representation; stock holder meetings are less opportunties for public input than they are opportunities to drum up more trade; and, the existing government oversight committees constitute a weak vehicle for public involvement.

POSSIBLE SOLUTIONS

The recent proposals by James B. Wyngaarden, MD, Director of the National Institutes of Health for a greater role of NIH in fostering biotechnology (Bio/Technology, November, 1985, p 1040). offer little promise for a more aggressive role of government in funding decisions. His suggestions to expand NIH's research support into the grey area between basic and applied research; to increase general support to the plant sciences; to increase the expertise in the U.S. in indUstrial bioprocessing; and to encourage more training of U.S. scientists outside of the U.S. restate the basically non-controversial objectives recommended by the Office of Technology Assessment to strengthen the U.S. domination of this field.

What is left unsaid in such pronouncements is how the government can better decide WHAT to fund and encourage in the private sector so that maximal public benefit--and minimum public harms--can be expected from biotechnological applications. A very small step in this direction has been to expand the umbrella of the Orphan Drug Act to encompass biotechnology-generated products (a stabilized form of alpha-1-antitrypsin for treating chronic obstructive pulmonary disease). But many of us in the public health sector would have liked to have seen more visible public support for vaccine development under the same guise, an avenue this Committee has recently actively considered.

The present public policy is not a public policy at all. Simply encouraging the broad-scale development of the biotechnology industry by facilitaing patenting and drug review processing rests on the blind hope that more will be necessarily better.

If the short history of this field is any guide, the strategems that have been followed have been guided by purely economic considerations. There is no assurance that more encouragement of this kind will generate those kinds of products that are vital to the public interest. I include in this latter category, vaccines; inexpensive and ecologically sound alternative energy sources; equally sound crop varieties that combine genetic resistance to pests with high protein yield; and relatively non-toxic pharmaceutcial products that complement or augment the therapeutic properties of naturally occurring biological substances.

What is needed now is a mechanism for both oversight and guidance for biotechnology so that these important and often critical areas of investment are selectively encouraged. Equally important are new mechanisms to reduce the dependency of the industry on secrecy. Encouraging more open disclosure and further facilitating patenting in favor of trade secrets are two first steps.

Public members are needed on oversight committees and institutional biosafety committees. Congress should consider whether or not a regulatory body modeled after the public utilitity commissions would be feasible and politically acceptable.

Putting more public input into the priority decisions made about funding in the public sector would also augment the process of de-privatizing a vital industry. It is also essential to the public value of this industry that young and budding researchers have the assurance that they will receive support for long-term research strategies for complex problems affecting public welfare.

Coordinating public input into the policy recommendations of Congress to encourage selected areas of research would also increase the likelihood of more applications that serve the public good. Basic research should be strengthened by offering protections and hence freeing data and information now held secret by biotechnology companies.

If carried out effectively, such strategies will ensure that project areas that serve the public good are also made economically viable and attractive. If done equitably, these new programs and policies will appeal to those who are most likely to take the risks needed to assure full production, namely those in the private sector who currently control the biotechnology industry itself.

Mr. Wyden. We thank you very much.
Mr. Nicholas.

TESTIMONY OF ROBERT B. NICHOLAS

Mr. Nicholas. I appreciate the opportunity to be here today to testify on the opportunities for the use of biotechnology and hazardous waste disposal.

To set the record straight, I am testifying today on my own behalf, not on behalf of any clients. I bring my expertise in following the biotech industry and hazardous waste disposal issues from the vantage point of the House Committee on Science and Technology where, until earlier this year, I was staff director and chief counsel of the oversight subcommittee. Previous to that position, I was counsel and senior staff member at the President's Council on Environmental Quality.

In the interest of time , I will keep my testimony short; and, at the conclusion, I will be happy to answer any questions.

In summary, there are three points I wish to make. The first point is scientific. Biotechnology can provide a tool to develop useful approaches for hazardous waste disposal.

The second point is economic. Development of biological approaches to hazardous waste control and cleanup have not been rapidly enough exploited because of the lack of appropriate economic and regulatory incentives, and because of the regulatory uncertainties surrounding the commercialization of biotechnology.

The third point is political. The Government needs to continue to provide incentives to encourage development of safe hazardous waste disposal technologies.

Biodegradation presents one promising alternative technology. Biodegradation is the use of micro-organisms to treat toxic chemicals and render them harmless.

According to OTA, once the technology is available, biodegradation is potentially less expensive than any other approach to neutralizing toxic waste. Such systems involve a low capital investment, low energy consumption and are often self-sustaining operations.

In biodegradation, the microorganism feeds on the toxic waste, or, in the presence of a particular waste, it will secrete an enzyme which dissolves the waste.

Using micro-organisms to degrade waste is not new. In many cases, the new skills of the genetic engineer in the laboratory may not even be required. Micro-organisms, which can degrade some of the most toxic chemicals, can be isolated from the soils of hazardous waste sites where these chemicals abound. These organisms can be selectively bred in the laboratory and returned as environmental scavengers to degrade the waste.

Recombinant DNA and other new biotechnologies can be used to enhance capabilities of existing strains or to engineer new genetic traits into microorganisms. The potential use for micro-organisms has been bolstered manyfold by the techniques of genetic engineering.

Biodegradation techniques are versatile and can be used at several different stages. For example, the removal of contaminants from raw materials before processing; the treatment of pipeline wastes before discharge from the factory; the decontamination of soils and surface and ground water; the cleanup of dump sites.

These operations may be conducted in a number of ways. Micro-organisms or their active products can be released directly into the contaminated environment. Micro-organisms already present in the environment may be enhanced by the addition of suitable nutrients. Micro-organisms may be used in contained or semicontained reactors.

Scientific problems will have to be overcome before many of the capabilities of biodegradation can move from a theoretical to a practical alternative. Biodegradation systems require that the appropriate micro-organism be developed; and also that a process technology be developed. The process technology makes possible the efficient and effective use of organisms in highly variable real world conditions.

Another significant area in need of research is that of what happens to the micro-organism after it accomplishes its task. This is not a particular concern when the organism is used in a contained vessel, but when it is released at a waste site significant questions arise about its transport and fate in the environment.

In summary, then, molecular biological approaches to hazardous waste control are scientifically promising. However, substantial additional basic science, process technology and environmental fate and monitoring questions will need to be undertaken before commercially viable approaches are developed.

The second point I want to emphasize is, that biodegradation has not developed as rapidly as it could, because of economic and regulatory disincentives. Government and the private sector are devoting some resources to enhance the effectiveness of biodegradation. It is difficult to develop a comprehensive overview, however. To date, there has not been, to my knowledge, a coordinated or sustained effort to undertake the basic scientific research, process technology or environmental fate and monitoring to support development of biodegradation.

A brief analysis of the Federal effort, which is contained in my statement, shows that research in this area is increasing, but the overall effort is relatively small. The Federal agencies have not made a substantial long-term investment in this area. It is perhaps not surprising that the commercial sector has not done so, either.

OTA has reported only a few cases where scientific research has progressed to a point where technologies are being developed by commercial concerns. There have been few reports of biotechnology companies entering this field. And OTA has concluded, in its 1984 report entitled "Commercial Biotechnology," that most companies will not fund biotech research on waste treatment.

The two principal reasons why biotechnology companies and others have not more actively pursued molecular biology for hazardous waste disposal are, one, a lack of economic and regulatory incentives to develop alternative technologies given the cheap cost of land filling; and two, the regulatory uncertainty concerning the conditions for use of genetically modified organisms introduced into the environment. To date, there has been little incentive to spend the capital and time to research and develop alternatives.

Much of the research needed to support biodegradation is basic or process technology. This research is long term and therefore costly and high risk. Other disincentives for the development of alternative technologies are discussed in the 1985 OTA report.

Congressional recognition of the need to promote alternatives to land filling of wastes is evident in the 1984 RCRA amendments and in the pending bills to reauthorize Superfund. The actions create new incentives to develop alternative technologies.

Without such direct encouragement, both as a policy direction and by providing financial support for basic and applied science, it is unlikely new technologies such as degradation can be developed rapidly.

The third point I want to emphasize is that the Government needs to continue its effort to support the development of alternative technologies for hazardous waste disposal. Several recent efforts provide new impetus to the development of biodegradation. These new authorities and programs will need to be effectievly coordinated both in and without the Government and creatively and fully implemented.

These programs include both Superfund and new joint research centers. In Superfund, both research and commercialization initiatives should be stimulated by new research, development, and demonstration programs. And in the interest of time, I won't review Superfund since many of you were very actively involved in and leaders in the House provisions.

With regard to the joint research centers, two centers have been established recently which could provide an additional impetus.

One, initially funded by an NSF grant for 5 years at $350,000 was established in New Jersey to develop hazardous waste disposal technologies. The other is at MIT, at a center, for bioprocess engineering. I will close now and I would be happy to respond to any questions the members may have.

[Testimony resumes on p. 74.]

[The prepared statement of Mr. Nicholas follows:]

OPPORTUNITIES FOR THE USES OF BIOTECHNOLOGY IN HAZARDOUS WASTE DISPOSAL

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Good Morning. I appreciate the invitation to be here today before this distinguished Committee to testify on the opportunities for the use of biotechnology in hazardous waste disposal.

My name is Robert B. Nicholas, and I am a partner in the Washington, D.C. law firm of Blum, Nash and Railsback. The firm is a general practice firm involved in regulatory, legislative and commercial matters. My practice involves biotechnology, environmental and other issues.

I am testifying today on my own behalf and not on behalf of any client. I bring here my experience in following the biotechnology industry and hazardous waste disposal issues from the vantage point of the House Committee on Science and Technology, where, until earlier this year, I served as Staff Director and Chief Counsel on the Oversight Subcommittee. Previous to that position, I was Counsel and then Senior Staff Member for Environmental Health and Toxic Substances at the President's Council on Environmental Quality.

In the interest of time, I will keep my testimony short and, at its conclusion, I would be happy to respond to any questions the members may have.

In summary, there are three points I wish to make:

1. The first point is scientific. Biotechnology can provide a tool to develop useful approaches for hazardous waste disposal;

2. The second point is economic. Development of biological approaches to hazardous waste control and clean-up have not been rapidly enough exploited because of the lack of appropriate economic and regulatory incentives and because of the regulatory uncertainty surrounding the commercialization of biotechnology; and

3. The third point is political. The government needs to continue to provide incentives to encourage development of safe hazardous waste disposal technologies.

To my first point: Biotechnology can provide a tool to develop useful approaches for hazardous waste disposal.

The Hazardous Waste Problem. To put my remarks in context, I want to discuss the hazardous waste problem in this country. I will do this very briefly since I know the members of the Subcommittee have played a very active role overseeing implementation of the hazardous waste laws and in the recent House reauthorization of Superfund.

Overall, the dimensions to the problem are large; answers are hard to find and solutions costly. Every year the 14,000 industrial plants in the U.S. generate some 265 metric tons of hazardous waste. The Environmental Protection Agency and the Office of Technology Assessment estimate that eighty percent of this waste is disposed of in land fills. Many of these wastes are toxic and long lasting in the environment. It is estimated, for example, that up to sixty five percent of all of the PCB's ever produced are still in the environment. Vast quantities of organic and inorganic compounds are in these disposal sites as well. These wastes, if not properly disposed of, can threaten the quality of our environment and the water supply. Accidental spills also present clean up problems. The costs to individuals, and to private industry and local, State and Federal authorities to deal with these problems are enormous. Some put the cost as high as twelve billion dollars a year. Given the volume of waste and the persistence of many of the wastes in the environment, land fills are at best only a temporary solution; development of alternative technologies that can destroy or lessen the toxicity or volume of hazardous waste are essential. The need to develop safe, effective and economic alternatives to the land filling of hazardous wastes has been reaffirmed by Congress in the RCRA Amendments, last year, and in the Superfund reauthorization this year. Biodegradation presents one promising alternative technique.

Biodegradation. Biodegradation is the use of microorganisms or their metabolites to treat toxic chemicals and render them harmless to human health. According the Office of Technology Assessment, once the technology is available, biodegradation is potentially less expensive than any other approach to neutralizing toxic wastes. Such systems involve a low capital investment, have a low energy consumption, and are often self-sustaining operations.

In biodegradation, the microbe feeds on the toxic waste or in the presence of a particular waste, it will secrete an enzyme which degrades the waste. Using microorganisms to degrade waste is not new. As early as 1914, researchers were isolating bacterial strains that efficiently degraded noxious sewage and reduced the total organic matter. In many cases the new skills of the genetic engineer in the laboratory may not even be required -- nature has beaten the scientists to the task. Microorganisms which can degrade some of the most toxic of chemicals can be isolated from the soil of the hazardous waste sites where these chemicals abound. These organisms can be selectively bred in the laboratory and returned as environmental scavengers to degrade the waste. RDNA and other new biotechnologies can be used to enhance the capabilities of existing strains, or to engineer new genetic traits into microorganisms.

The potential use for microorganisms in hazardous waste disposal has been boosted many fold by the techniques of genetic engineering and the subsequent understanding of how to direct microorganisms to degrade a whole range of chemicals which do not occur naturally in the environment. The gambit of toxic substances that can potentially be degraded by microorganisms is limited now only by our ability to isolate the genes for the microbial enzymes which break these compounds down.

Biodegradation techniques are versatile and can be used at several different stages. For example, for:

-- the removal of contaminants from raw materials before processing (e.g., desulphurisation of coal before it is burned prevents acid rain);

-- the treatment of pipeline wastes before their discharge from the factory;

-- the decontamination of soils and surface and ground water; and

-- the cleanup of dumpsites.

These operations may be conducted in a number of ways:

-- microorganisms or their active products can be released directly into the contaminated environment;

-- microorganisms already present in the environment may be enhanced by the addition of suitable nutrients (bioaugmentation); and

-- microorganisms may be used in contained or semi-contained reactors.

Biodegradation presents a clearly attractive alternative to the land filling of hazardous waste and for the clean-up of wastes. However, scientific problems will have to be overcome before many of the capabilities of biodegradation can move from a theoritical to a practical alternative.

Biodegradation systems for hazardous waste treatment require that appropriate microorganisms be developed -- microorganisms that can biodegrade the waste -- and also that a process technology be developed.[1] The process technology makes possible the efficient and effective use of microorganisms in highly variable, real world conditions. Two of the most significant scientific problems hindering more extensive development of biodegradation as a technique for treatment of hazardous waste include learning more about catabolic pathways, that is, the pathways used by microorganisms to breakdown the waste and more about how microorganisms survive in the environment.

The prospects for constructing or finding in nature the catabolic pathways to effect the detoxification of hazardous chemicals are encouraging. There are many sources of catabolic genes:

-- in vitro genetic engineering;

-- laboratory selection techniques;

-- naturally occurring organisms;

-- environments as yet untapped (extreme, anaerobic, marine).

Developments in this area will depend on an increased understanding of microbial physiology, the basic biochemical and genetic bases for microbial detoxifications, and on an understanding of microbial resistances to heavy metals. The microbial degradation processes also must be made to work fast enough to be of practical use, so information is needed on the kinetics of bacterial growth and biodegradation.

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[1] See generally, Ghosal, et al, "Microbial Degradation of Halogenated Compounds", Science, v. 228, No. 4696 (12 April 1985), attached as Appendix A.

For the control of environmental pollution, organisms must have not only the correct catabolic potential, but also the full array of ecologically important traits needed for success in the environment -- that is, the useful organism must have a competitive advantage over the indigenous organisms so that they will survive long enough to accomplish their task. It is possible that this may require genetic manipulation on ecologically important traits.

There are other problems to be overcome in developing suitable microorganisms:

-- any one bacterial strain will generally degrade only one particular chemical or closely related groups of chemicals. However many of the wastes to be treated will contain a number of toxic chemicals in varying concentrations. The open literature contains little work on using microorganisms to treat complex waste mixtures;

-- in many cases, there will be carbon sources present which will be utilized by the microorganisms as nutrient sources in preference to the desired toxic chemical;

-- no microorganism has yet been shown to grow on a defined substrate at concentrations at which pollutants are frequently of practical concern (10 ppb);

-- in open systems the effectiveness of the technology will be influenced by environmental conditions such as temperature, type of soil, presence of other naturally occurring microorganisms, and presence of water and oxygen and acidity;

-- since many of the constituents present in the waste pool are mutagens, the organism could mutate to an ineffective strain.

The development of the various uses of biodegradation will require a multidisciplinary approach, using the combined skills of microbiologists, physiologists, ecologists, biochemists, molecular biologists and engineers.

In the past few years, there have been some exciting reports from researchers about the potential for microorganisms to degrade hazardous waste under laboratory conditions. To date, some forty bacterial strains and species have been isolated that between them are able to degrade many of the compounds of the greatest concern, although in many cases degradation is not fast enough to be of practical interest. The compounds include most all of those of major concern:

-- organophosphate pesticides such as parathion and malathion;

-- other pesticides such as carbofuran and alachlor;

-- DDT, carbon tetrachloride and other halogenated hydrocarbons;

-- 2,4-D, 2,4,5-T and dioxin;

-- PCB's

-- benzene, toluene, biphenyls and naphthalene;

-- heavy metals such as mercury, cadmium, uranium and selenium and their organic derivatives.

As I noted before, however, there is a major gap between the laboratory studies and the applied technology. The laboratory development of useful bacterial strains does not appear to be sufficiently closely linked to process engineering in order to capitalize on the growing market opportunities.

Another question that must be addressed before micro-organisms can be used in other than a contained environment is that of what happens to the organism after it has done its work. Additional research needs to be undertaken in predictive ecology to better insure that this solution to waste disposal does not unintentionally create new and serious environmental problems.

In summary, molecular biological approaches to hazardous waste control are scientifically promising. However substantial additional basic science, process technology and enviornmental fate and monitoring research will need to be undertaken before commercially viable approaches are developed.

The second point I want to emphasize is that biodegradation has not developed as rapidly as it could because of economic and regulatory disincentives.

Government and the private sector are devoting some resources to enhance the effectiveness of biodegradation as a technique for waste disposal. It is difficult, however, to develop a comprehensive overview of these efforts because the work is fragmented and much of what is going on may be proprietary.

To date there has not, to my knowledge, been a coordinated or sustained effort to undertake the basic scientific research in molecular biology, process technology or environmental fate and monitoring to support development of biodegradation as a hazardous waste technology. A brief analysis of the research efforts of the Federal agencies shows an increasing but relatively small effort. The pending reauthorization of Superfund would provide, however, a new focus and impetus for development of alternative and innovative technologies.

The current situation is this: Since 1981, EPA has funded twelve projects in this area (five projects on municipal waste water biological treatment and seven projects on hazardous waste chemical and biological detoxification). The U.S. Department of Agriculture has a research team looking at pesticide degradation, and this team has recently been expanded by the addition of molecular geneticists. The Department of Interior and the Department of Energy have interests in biodegradation and closely allied areas such as using bioaccumulation techniques to concentrate metal ions and the desulphurisation of coal. These agencies are currently funding perhaps four projects. The Department of Defense, as a generator of hazardous waste faces significant disposal problems. The Department of Defense is looking at ways to remove toxic substances such as agent orange from the environment. During 1983 through 1985, the Air force, together with EPA, funded one research project (to a level of $150,000) to investigate in situ detoxification by microorganisms of soil contaminated with agent orange.

If the Federal agencies have not made a substantial long term investments in this area, then it is perhaps not surprising that the commercial sector has not done so either. OTA has reported only a few cases where the scientific research has progressed to a point where technologies are being developed by commercial concerns. The 1985 Office of Technology Assessment report on Superfund Strategy documented four technologies which used biodegradation. They involved in situ biological treatment of PCB's in soil, decontamination of groundwater by bioaugmentation and a sequencing batch reactor. Other companies are looking to develop plant pollution control systems using microorganisms. Some of the large companies, with significant on-site disposal and in-house scientific expertise are undoubtedly exploring molecular biological approaches. All these companies are looking cautiously at commercialization. There have been few reports of biotechnology companies entering this field, and OTA has concluded in its 1984 report entitled, Commercial Biotechnology, that most companies will not fund biotechnology research on waste treatment. To date, much of the research interest and funding, both private and governmental, has been directed towards the microorganisms, with only limited funding to developing the technology.

The two principal reasons why biotechnology companies and other have not more actively pursued molecular biology for hazardous waste treatment are:

1. A lack of economic and regulatory incentives to develop alternative technologies, given the cheap cost of land filling; and the

2. regulatory uncertainty concerning the conditions for use of genetically modified organisms introduced into the environment.

To date there has been little incentive to spend the capital and time to research and develop alternatives to land filling of hazardous wastes. Much of the research needed to support biodegradation is basic or process technology. This research is long term and therefore costly and high risk; it is not the type of research ordinarily undertaken by most companies, and clearly not the research undertaken by the small innovative biotechnology companies. Other disincentives for the development of alternative waste disposal technologies such as degradation which were identified in the 1985 OTA Superfund report include policy and market uncertainties; absence of adequate RD&D funding; institutional practices and regulatory impacts; status quo bias regarding existing technologies.

Congressional recognition of the need to promote alternatives to land filling of wastes evidenced in the 1984 RCRA Amendments, and in the pending bills to reauthorize Superfund, clearly create new incentives.

Without such direct encouragement -- both as a policy directive and by providing financial support for basic and applied science -- it is unlikely that new technologies can be rapidly developed. An analogy in the biomedical field is perhaps relevant. Only because NIH and, to a lesser degree, the National Science Foundation, were given the mandate and funds by Congress to support basic biomedical research, were the crucial discoveries made in the basic science, that allowed the development of biotechnology, and the enormous potential commercial and public benefits now on the near horizon.

Another reason to encourage and support process engineering and basic molecular biology to enhance waste disposal technologies is that it could also provide additional understanding about the behavior of organisms in the environment. This information could prove useful to companies seeking to develop additional uses for genetically modified organisms which would present environmentally safer alternatives to existing products, such as the development of biorational pesticides to replace chemical pesticides. In addition, new information would assist in the development of a predictive ecology to help answer some of the regulatory questions.

The uncertainty in the regulatory picture concerning field testing of genetically engineered organisms has provided a disincentive to enter this field. It is difficult to justify large expenditures when uncertainty exists as to whether or not the modified or selected organism will be allowed to be tested. Recently, EPA and NIH have approved field tests of genetically modified organisms and the regulatory picture, though still unclear, should move closer toward resolution with the anticipated January publication of the revisions to the Cabinet Council policy statements, originally published in December 1984.

In summary, regulatory and economic disincentives have tended in the past to discourage development of biodegradation.

The third point I was to emphasize is that the government needs to continue its efforts to support the development of alternative hazardous waste technologies.

Several recent efforts of the government provide new impetus for the development of biodegradation and other hazardous waste disposal technologies. These new authorities and programs will need to be effectively coordinated, both in and without government and creatively and fully implemented. These programs include:

1. Superfund. Both research and commercialization initiatives should be stimulated by the new research, development and demonstration provisions in Superfund. This program will

provide funds for research and development into new technologies for cleaning up hazardous wastes through both Health and Human Services and the Environmental Protection Agency. Commercial development of alternative and innovative technologies should be stimulated, because EPA is will now be required to provide for the demonstration and evaluation of approved projects at hazardous waste sites. This latter provision I know is one that industry eagerly sought. Superfund also recognized that new technologies are needed -- that merely storing toxic wastes or cleaning up Superfund sites by removal of wastes to another site are hazardous shell games.

2. Joint Research Centers. Two centers have been established recently which could provide additional impetus for development of biodegradation. One, initially funded by an NSF grant for five years of $350,000, was established to develop hazardous waste disposal technologies. The Industry/University Cooperative Research Center for Hazardous and Toxic Waste at the New Jersey Institute of Technology in Newark was set up in October 1984 and is designed to pool the talent and funds of the private sector, government and academia. The other center, while not directed toward waste disposal technologies, is the joint NIH/NSF center for bioprocessing engineering at MIT.

It is too soon to tell whether these and similar new initiatives will be sufficient, but the government is clearly on the right track. The effective coordination of Federal research efforts and a commitment to some long term research in this area is what is needed. The concerned industries -- those who could benefit most from biodegradation technologies -- also need to take an important lead. The coordination and pooling of research and development resources benefit all in terms of rapid development of new and potentially safer, more effective and less costly technologies.

In conclusion, while much remains to be done to develop waste disposal technologies, I am optimistic that biodegradation will not remain an undeveloped technology.

Mr. WYDEN. Mr. Nicholas, we thank you. I think you know I am a Member of Congress particularly interested in this area. I have felt for a long time programs like Superfund are essentially maintenance programs, and what we are doing is shuffling these dangerous wastes from one site to another, almost the toxic waste merry-go-round and you give us insight as to how we might get off that merry-go-round and produce these wastes in the first place and make them less dangerous.

We will have some questions for you momentarily.

Dr. Novick, thank you for your participation today. We look forward to any remarks you may have.

STATEMENT OF RICHARD P. NOVICK

Mr. NOVICK. Mr. Chairman, my name is Richard Novick. I am a molecular biologist and director of the Public Health Research Institute in New York City. I thank the subcommittee for the opportunity to testify on this important question this morning.

In contrast to the previous speakers, the area I wish to discuss; namely, the question of the impact of biotechnology on potential biological warfare and weapons development is much hazier and grayer.

Given a situation where there is more heat than light, one is driven to interpret available data rather liberally and I beg your indulgence as I do so.

I wish to cover four points this morning.

One, biological weapons and warfare cannot be defended against in any but a very limited manner.

Two, biological weapons are useless in open warfare.

Three, biological weapons may be very useful for covert operations; and

Four, it is this area in which I believe the advent of recombinant DNA technology may have a significant impact in the present and near future.

My own personal concern over the possible use of recombinant DNA in biological weapons development dates from the 1974 Asilomar Conference on the potential hazards of recombinant DNA.

As chairman of a committee known as the Plasmid Working Group at Asilomar, I was responsible for the preparation of a proposal which was to form the basis of the National Institutes of Health guidelines for recombinant DNA research.

Recognizing that the development of biological weapons was perhaps the most serious imaginable hazard of genetic engineering in that it was the purposeful creation of dangerous organisms, the committee urged in its proposal that, the construction of gentically altered microorganisms for military purposes be expressly prohibited by international treaty.

As no such prohibition yet exists, I remain concerned, and my concern has not abated following the 1972 convention on biological and toxin weapons whose language does not contain such an express prohibition but rather leaves much room for creative interpretation.

Indeed, I shall discuss evidence suggesting there is currently a resurgence and military interest in bioweapons based on the exploitation of recombinant DNA technology.

I will focus on this country not because I have any doubts that there are activities elsewhere, but rather because what little information I have is based on local activities.

Before proceeding further, I would like to remind the committee that genetic engineering or gene splicing involves the isolation of specific DNA molecules that encode the information for the production of a particular biological product followed by the statement in the test tube to transfer these DNA molecules to a species of DNA known as a plasmid.

The resulting plasmid or chimera is what is referred to when one speaks of a cloned gene. This composite plasmid is placed in a bacterial strain in which it is capable of replication and in which the product of the cloned gene can be produced. This product may become a part of the organism's genetic makeup or may be released into the environment, for example, as a toxin.

The question then is, what can this ability to develop novel genetic combinations artificially offer to one who wishes to engage in biological weapons development? It must be recognized at the outset, in view of prohibitions on the development of offensive biological weapons, that any such program must necessarily be listed or viewed as defensive.

However, as there is no substantive difference between offensive and defensive biological weapons research, the distinction must really be considered as a matter of intent. I would give an example. As you may know, Fort Dietrich is currently developing a vaccine against a virus known as the Marburg virus. This is one of the world's most deadly, but one that poses little, if any, threat to U.S. troops. This could be considered as a defensive measure in anticipation of the use of the virus by some adversary as a biological weapon or considered as a necessary component of any program to develop the virus itself for offensive use, the distinction can't be made externally.

In any event, even given a purely defensive concern, can one envision a credible antibiowar defense, and, if so, would such a defense involve the development by recombinant DNA techniques of new potentially offensive weapons systems against which to build that defense? Realistic defenses against biological weapons would involve primary physical protection such as that used against poison gas plus prophylactic or curative treatment, such as vaccines or antibiotics.

These measures would be coupled with an identification system to discover that one is being attacked in the first place. Physical protection would be effective but would be practical only for troops in the field and would be based, of course, simply on the exclusion of the infected particles. Nothing could be gained by the use of genetic engineering to develop novel particles to test such equipment since protection is based on the size and other physical characteristics of the particle, and these could not be altered genetically.

Even before the recombinant DNA era, it would have been a task of tremendous magnitude to develop and stockpile vaccines against all possible biological warfare agents sufficient for mass vaccination of the entire population. Even that, however, would have been of little use against an effective surprise attack, since a vaccine must be given well in advance of exposure to the organism.

With the advent of recombinant DNA, the possibility of an effective vaccine defense has become even more remote. Since one could develop an infinite number of immunological variants by modifying and transplanting genes, there is no way to anticipate what a determined adversary might develop. This is an important point. There is no way one could mount a defense against this sort of adventurism. Any attempt to develop modified biological warfare agents in order to anticipate enemy action is an exercise in futility and simply cannot be justified on the grounds of defense.

A similar argument would hold for detection systems. While technology already exists for the physical detection of infectious particles in air or water, their identification would be a task of unimaginable difficulty in the recombinant DNA era and, again, anticipatory research would be an exercise in futility.

For reasons such as these, military programs involving recombinant DNA or involving the development of vaccines against rare and deadly pathogens, especially if any of it is secret, would inevitably destabilize any international détente vis-a-vis biological warfare and could lead to a rapid multilateral escalation.

The best means of avoiding suspicion is to conduct all biological research in the open, preferably in the civilian sector. The fact that biological warfare is undefendable should not, however, be any cause for alarm. As recognized by President Nixon in 1969, when he took the bold initiative of unilaterally abandoning biological weapons even in retaliation, biological weapons are inherently useless in open warfare.

This is because they are highly unreliable and unpredictable, subject to great variability in attack and survival rates, and to great uncertainty due to environmental conditions. They can spread out of control and initiate epidemics in civilian populations on either side and can readily backfire locally; their use would be met with universal repugnance and would be likely to trigger a nuclear response.

For the same reason, biological weapons would not serve as any sort of deterrent. Surely, the nuclear shield would very effectively deter biological adventurism. But if biological weapons are militarily useless, why the renewed interest? I would suggest that covert operations and terrorism are much more appropriate arenas for biological warfare than open strategic or tactical activities on the battlefield.

In a covert operation, one might go after a potential adversary with whom one is not at war and in a situation where overt military action would be unacceptable. The most obvious application would be the undermining of a small nation by a larger one desirous of removing or replacing that country's government. Here, the biological agent would be used to create an epidemic or to destroy crops or livestock; it would have to be of a type that could plausibly occur locally and could be released in a manner that would avoid detection of the attacker. One must not get caught in such an adventure.

Here, perhaps is the most attractive potential for rDNA. One would modify the immunological properties of the agent—most probably a virus in this case—so as to bypass the natural immunity of the target population. One could then immunize any friendly elements and proceed with the attack. It will be recalled that this model was used, albeit inadvertently, with remarkable success against the native American by the European settlers.

Probably 90 percent of the local population was killed by diseases such as smallpox and syphilis; diseases against which the settlers were largely immune and which were inadvertently into the native population.

Terrorism is another cause for real concern, for obvious reasons, though not especially with regard to recombinant DNA. Fortunately, thus far, terrorist groups have not adopted any such strategy; again, as with other forms of biological weapons, it would be difficult to defend against.

I have alluded to renewed interest in weapons. I would like to mention in the context of my previous remarks a few of the items that have aroused concern. As you may know, currently in progress in Government installations are a number of projects that one would like to scrutinize somewhat more carefully. Among these are the development of vaccines against rare viruses of exceptional virulence, the development of vaccines against bacterial toxins, the development of vaccines against highly pathogenic rickettsia, the actual study of bacterial toxins, the cloning of bacterial toxin genes into foreign bacterial species, and the cloning of acetyl cholinesterase genes, whose product would be a nerve gas antidote.

Most of these items are represented as purely defensive. The argument that defense versus offense is purely a matter of intent applies to these as well. In addition to these items there are two others that I find more difficult to defend or to define as possibly defensive. The first of these is the planned facility for aerosol testing at Dugway Proving Ground. In my view, the Army has failed to make a convincing case for need to construct a new aerosol laboratory at Dugway for purely defensive purposes.

This view is shared by many scientists and was discussed widely in the press earlier this year. I would be happy to elaborate on this point if the members so desire after my testimony is complete. More disturbing, if admittedly the most speculative of the points I wish to make this morning, is the appearance in the Wall Street Journal and the Washington Post during early 1984 of a series of highly inflammatory articles purporting to show that the U.S.S.R. is involved in an extensive program to develop new biological weapons by use of genetic engineering technology.

The most inflammatory of these was a column by Jack Anderson in the Washington Post, February 21, 1984, of which I have included copies for your perusal. One's suspicions as a scientist were aroused by a series of glaring errors and obvious fabrications in this and the other articles, which I would be happy to elaborate on afterwards.

The Anderson article was based on a secret CIA document. The most disturbing thing about this and the other articles is that it strains one's credibility to the breaking point to imagine that CIA was unaware of the gross factual errors contained in them. One is forced to conclude that the articles were planted and that they constitute an example of the now classical missile gap ploy in which a fictitious weapons technology gap is created in the mind of the public in order to soften the opposition to yet another escalation of the arms race.

One might speculate further that the new Dugway lab, which was publicly announced soon after the appearance of these articles, could well have been the objective of this ploy. I would conclude by saying that I believe there are grounds for concern over the possibility that the United States and perhaps also the U.S.S.R. are about to initiate research into offensive biological weapons, based on allegations that the other side is doing so, and there is no choice.

Nevertheless, I believe President Nixon was entirely correct in his assessment that biological weapons are not a credible threat to U.S. security, or to U.S.S.R. security, and that it is of no direct concern to either power what the other is doing in this area. Rather, the development of biological weapons, with or without gene splicing, should be of concern to smaller nations, particularly those of the Third World, who could be the object of covert attacks by either of the major powers.

I would like to thank the committee for its attention to these remarks, and I will be happy to answer any questions.

[Testimony resumes on p. 104.]

[The prepared statement and attachments of Mr. Novick follows:]

THE POSSIBLE IMPACT OF GENETIC ENGINEERING TECHNOLOGY ON THE DEVELOPMENT AND USE OF BIOLOGICAL WEAPONS

By Richard P. Novick, M.D.
Director
The Public Health Research Institute of the City of New York, Inc.

Mr. Chairman, members of the Subcommittee, my name is Richard Novick; I am Director of the Public Health Research Institute, a private, non-profit institution devoted to research in basic biomedical sciences with a focus on problems of infectious diseases. I would like to thank the Subcommittee for inviting me to testify on the implications of biotechnology for biological warfare, a subject that was of major concern to me even before the first gene splicing experiments were performed back in 1972.

This concern stems primarily from my own work with *Staphylococcus aureus*, a pathogenic bacterial species which is of military interest because of its resistance to antibiotics and its ability to produce enterotoxins - both of which could readily be transferred to other bacteria. I have twice been invited to accept DOD funding for my work and have declined because I believe strongly that the fruits of research in the life sciences should not be used for military purposes and that the DOD should not be in the business of funding biomedical research in the civilian sector. I would like to state my own position on biological weapons clearly at this point: this is that I believe that the development of biological weapons is an egregious misuse of the science of life and cannot be condoned by any entity for any purpose, including "defense".

As chairman of the "Plasmid Working Group" for the historic 1974 Asilomar meeting on the potential hazards of the new technology, I was responsible for guiding the preparation of a proposal which was to form the basis of the NIH Guidelines on Recombinant DNA Research. Recognizing that the development of biological weapons was perhaps the most serious imaginable hazard of genetic engineering, we urged that "the construction of genetically altered microorganisms for military purposes be expressly prohibited by international treaty". This provision was not adopted by the Asilomar meeting nor has it ever been included in the Guidelines, because these were both focussed sharply on laboratory safety and expressly avoided any type of political or moral issue.

As the 1972 Convention on Biological and Toxin Weapons predated the invention of rDNA technology, there has always been doubt about whether it covered the new technology adequately. Indeed, as I will show shortly, there seems to have been a recent resurgence in military interest in bioweapons, primarily through the exploitation of rDNA technology. Because of this resurgence, Prof. Richard Goldstein and I proposed in 1982 that the National Advisory Committee on rDNA (RAC) incorporate into the Guidelines just such a prohibition. Again, the proposal was defeated, the Committee stating that it would tend to undermine the Convention, which it saw as adequately covering any military application of rDNA, and was beyond the jurisdiction of the Committee, in any case.

Before I get into the main body of my testimony, I would like to remind you that genetic engineering involves the isolation of specific DNA molecules that encode the information for the production of a particular biological product followed by the attachment in the test tube of such molecules to species of carrier DNA -

usually a bacterial plasmid. The resultant composite plasmid or chimera is what is referred to when one speaks of a cloned gene. The composite plasmid is then emplaced in a bacterial strain in which the plasmid is capable of autonomous replication and in which the product of the cloned gene can be produced. In some cases - insulin, growth hormone, interleukin, etc. - one will have achieved a means of producing large quantities of a rare and important substance. In other cases - botulin toxin, enterotoxin, diphtheria toxin - one will have a novel organism that produces in large quantity a specific substance of military interest. In still other cases, random segments of DNA from a disease-causing organism could be introduced into a second species and the recombinants tested for the acquisition of disease-causing ability. These sorts of experiments would permit the identification of specific genetic functions that are involved in the causation of disease and would thus be of major medical interest; as they would also create novel organisms with modified disease-causing potential, they could be of major military interest. Parenthetically, it is very unlikely for biological reasons that such a hybrid bacterial organism would be more pathogenic than either of the parental species from which it was derived; rather, it might combine certain desirable characteristics of one species - immunological properties, survival characteristics - with the disease-causing potential of the other and so make a more effective biological weapon.

My presentation is in four main sections - I will consider first a number of basic questions, then list the overall possibilities for biological weapons and consider specific types of biological modifications of microorganisms and finally review the available evidence for renewed activity in biological weapons development and defense.

I. Major questions

A. Is it possible to distinguish offensive from defensive research involving bioweapons?

No - this is purely a matter of intent. For example, the development of a vaccine against Marburg virus, one of the world's most deadly, and one that poses little, if any natural threat to US troops, could be considered as a defensive measure in anticipation of, the use of the virus by an adversary, or it could be considered as a necessary component of any program to develop the virus for offensive use.

B. Must new potentially offensive weapons systems be developed in order to develop defenses?

In answer to this question, it should be noted that defenses may be physical or biological and that one of the attractive potentials for genetic engineering is the possibility of circumventing biological defenses. It is argued that physical defenses such as protective clothing are not at issue here, since these must be capable of protecting against any imaginable agent. Although biological defenses such as vaccines must be highly specific, it is argued that it would be completely impossible to anticipate the immunological properties of any genetically engineered agent - thus any research conducted under the guise of being anticipatory must be viewed as purely offensive in actual intent.

C. What are the possibilities for anti-bioweapons defense?

My view is that troops in the field would have to rely on protective clothing; vaccines would be useful only in the face of positive intelligence with respect to the nature of the agent; treatment with drugs such as antibiotics would be useful only for bacteria and only after the isolation and testing of the organism. It is virtually inconceivable that a civilian population could be protected against a surprise biological attack unless one knew with certainty the identity of the agent and could therefore administer the appropriate vaccine. The same argument would hold for livestock; I am unaware of any type of protection or defense that could be used for crops and other plant life.

D. What are the international consequences of programs to develop vaccines against the deadliest pathogens?

If one accepts the argument that effective defenses in the age of genetic engineering are unlikely in the extreme, then one must view any program of research involving potential biological agents of warfare of this type as offensive in intent. This vision is likely to have a severe destabilizing effect at an international level, causing any nation that perceives such programs in the hands of a potential adversary to undertake similar research - leading to a biological arms race, which would be both dangerous and futile.

E. Can classified research on biological weapons systems or defenses be justified?

The best means of avoiding suspicion is to conduct all research in the open; we are told that development of detection systems, for example, must be kept secret as the enemy could develop means of circumventing them. Unfortunately, on the one hand, a comprehensive system for the detection and identification of all possible agents is unimaginable; on the other hand, the principles of general detection are obvious enough and a reasonably sensitive system cannot be circumvented.

F. What is the relation between President Nixon's unilateral renunciation of biological weapons and present interest as articulated in the press? Was Nixon's initiative premature or in error?

In my view, President Nixon's initiative was a bold, imaginative and appropriate move and nothing has happened to engender any second thoughts in my mind; the idea of unilateral renunciation is predicated on the principle that one is entirely unconcerned with any possible action by a potential adversary; as discussed below, the advent of genetic engineering cannot alter the fact that biological weapons have no place in open warfare and they are useless as a deterrent.

G. Is there a serious question regarding USSR compliance with the 1972 Biological Weapons Convention and, if so, what should be done about it?

The ideal of a reliable system of verification is one that should be pursued vigorously; unfortunately, since offensive and defensive research would utilize the same type of facility, which could also be used for entirely innocent civilian research, it could be very difficult to establish intent. Fortunately, since biological weapons are of no use in any overt military conflict, violations of the Convention will do the violator great harm because of local dangers and because of adverse public opinion, without posing any credible strategic threat. I believe it would be effective merely to publicize violations (but only if the documentation is impeccable); abrogation or retaliatory violations could serve no useful purpose.

II. Potential uses of gene-spliced bioweapons. Crops and livestock or personnel or both can be targeted in most of the following applications.

A. Military - open warfare

1. Strategic - international, intercontinental.

The reason that President Nixon unilaterally renounced the use of biological weapons, even in retaliation, and abandoned the US development program is that he was convinced that they were inherently useless in warfare. This is because they are highly unreliable and unpredictable, subject to great variability in attack and survival rates, and to great uncertainty due to environmental conditions. They can spread out of control and initiate epidemics in civilian populations on either side and can readily backfire locally; their use would be met with universal repugnance and would be likely to trigger a nuclear response.

2. Tactical - local battlefield; theater.

The same arguments apply, for the most part, to local as to strategic conflicts. One exception is that the threat of a biological attack would require cumbersome protective clothing, etc., which would hamper mobility of troops. This would gain no advantage as it would shortly affect both sides. In my view, the application of genetic engineering technology would have no significant impact on any of these considerations - the basic nature of infectious microorganisms cannot be changed by this or any other technology.

B. Military - covert warfare.

By covert warfare is meant an attack whose source cannot be identified. Here, one would release a bioweapon surreptitiously to undermine the adversary's troops or civilian population. This type of operation is conceivable; however, the danger that the source might be identified, with possible nuclear consequences, would seem to superimpose an unacceptable risk factor upon an action of dubious effectiveness.

C. Paramilitary - subversion.

By subversion is meant the undermining of a potential adversary with which one is not at war and in a situation where overt military action would be unacceptable. The most obvious application would be the undermining of a small nation by a larger one desirous of removing or replacing that country's government. Here, the biological agent would be used to create an epidemic or to destroy crops or livestock; it would have to be of a type that could plausibly occur locally and could be released in a manner that would avoid detection. In my view, this application (plus terrorism - see below) is the most attractive and the most probable for genetically engineered bioweapons.

D. Terrorism.

The possible use of bioweapons by terrorists is certainly a terrifying prospect and one to which no population group would be immune. The possibilities are obvious enough; here, however, one need not be concerned about genetic engineering since any imaginable terrorist objective would be very adequately served by existing microorganisms; additionally, it is not likely that most terrorist organizations would have the scientific sophistication necessary to perform gene splicing and then test the results. Parenthetically, it seems odd that terrorism has not yet hit upon this strategem and one would suppose that this is only a matter of time. Whether anything could be done in the way of prevention or defense seems rather doubtful.

III. Possible applications of gene-splicing technology to bioweapons development (note that many of the following modifications could be achieved in principle by conventional microbiological methods and that it is not always obvious how gene splicing could be applied).

A. Develop pathogenic organisms more virulent than those now known.

It is difficult to imagine the creation of a disease-causing organism that is more deadly than any now known and so it makes very little sense to attempt any such project by genetic engineering or any other means. Additionally, the ability to cause disease is due to a highly complex set of very poorly understood biological traits and as current knowledge does not encompass the understanding of this for any organism, it is most improbable that anything effective could be accomplished; any attempt to "improve" an organism's disease-causing ability genetically is likely to interfere adversely with the highly developed and integrated pattern of characteristics that constitute pathogenicity.

B. Modify existing pathogenic organisms so as to improve their utility as weapons.

I believe that this is the most important area for concern because one can readily envision potentially effective applications for genetic engineering. Because one could rarely, if ever, be certain that a projected modification would have the desired effects, a great deal of laboratory research and testing would have to be done and this would inevitably involve human subjects at some level. It is difficult to imagine that animal data would ever be sufficient; as the initiator of a biological attack, I would be very uncomfortable about releasing a novel pathogenic organism whose effects on humans were unknown. Nevertheless, it may be useful to consider the types of experiments that could be envisioned. The ideas here, however, must be regarded as entirely speculative.

1. Modify physical characteristics - e.g. improve ability to survive as aerosol; increase (or decrease) ability to survive in environment.

I will give one example - many others could easily be imagined. One important means of dispersal of biological agents is by means of aerosols; organisms contained in aerosol particles are sensitive to various adverse environmental factors such as dessication and radiation. Certain bacteria are highly resistant to radiation and this resistance is thought to be due to a relatively small number of genes. These genes could be transplanted into a pathogenic organism with the intention of improving its ability to survive the radiation it would receive when aerosolized.

2. Modify biological characteristics - e.g., change host range: create "ethnic" weapons.

Those interested in the possibility of biological weapons have occasionally expressed an interest in developing a pathogenic organism that was specific for a particular racial type. Whether this is possible is presently unknown; a great deal of research would have to be done to locate organisms that have any degree of racial preference and then to attempt to identify and isolate any genes that might be involved in this preference. By combining such genes from several different microorganisms, one might hope to develop a fully race-specific pathogen. Again, this would involve extensive testing with human subjects and would therefore be very difficult for any civilized country.

3. Modify immunological properties - change antigenic specificity.

This would seem to me to be the most attractive application of gene splicing to biological warfare. It would involve primarily viruses since the substances that evoke protective immunity are usually proteins that are located on the surface of the virus particle and are relatively easy to identify. Here, one would replace the gene for an immunity-evoking surface protein with a similar gene from a related virus. This happens spontaneously with influenza virus and is a common and problematic characteristic of this virus. The modified virus would then bypass any natural immunity in the target population while the attacker could easily immunize any of its own personnel that might be exposed. This would clearly be the ideal way for a large nation to undermine a smaller one by covert biological warfare, especially if there were an indigenous sympathetic group. Again, much research would have to be done, partly with human subjects, as there would be no guarantee that the modified virus would still be infective.

4. *Introduce toxin genes into non-toxigenic bacteria.*

The "classical" biowar scenario for gene splicing would be to transplant the gene for botulin toxin into *Escherichia coli*. One could then contaminate the water supply of an enemy with a common organism capable of producing the deadliest poison known. It is fortunately doubtful that such an organism would perform as desired, primarily because *E. coli* does not secrete protein products into the surrounding environment and secondarily because toxins are characteristically produced by bacteria only during luxuriant growth - which would not be the case even in a relatively dirty water source; although in principle such an organism could be used with effect only in a country with poor sanitation and public health practices, no sane government would contemplate releasing it because once released there would be no way to control its spread and it could easily turn up anywhere in the world. Other possibilities might involve diphtheria toxin, staphylococcal enterotoxins, or ricin and might employ *Streptococcus fecalis*, a potential water contaminant that does secrete proteins. As with the other types of experiments that could be contemplated, much laboratory work would be required to establish effectiveness. With toxins, however, one would not require human subjects.

In balance, the use of toxin-producing organisms does not strike one as a particularly effective means of delivering an active dose of toxin to a large number of people in a short time - rather, one would probably use the toxin itself and one could surely use genetic engineering technology to develop a bacterial strain capable of producing any toxin in much larger amounts than those produced by the native organism. This, however, would provide an advantage only in production.

A more novel approach with toxins would be to create hybrid molecules by genetic engineering. Here, one would splice two or more genes or parts of genes to produce a protein with a structure that was any desired combination of other proteins or parts. The possibilities are limitless here; hybrids between toxin and antibody molecules have been constructed with the purpose of targeting the toxin to cells, such as cancer cells, recognized by the antibody. Here, conceivably, might be an opportunity for the development of an "ethnic" weapon - one would first have to identify a protein specific for a particular population group, develop an antibody against this protein, then connect this to a toxin by gene splicing. The construction would have to be cleverly engineered so that the toxin would be activated only as a consequence of the reaction between the antibody and targeted protein. This idea, at present, would have to be regarded as science fiction/fantasy; however, one could envision an experimental program to explore it. Additionally, rumors have been heard from time to time that experimentation was afoot to construct double or triple toxin molecules as weapons. I am not aware of any substantiation of such rumors nor can I envision any obvious advantage that such molecules might have over the individual toxins.

IV. Known or suspected current activities in bioweapons development and defense.

A. Development of vaccines against rare viruses of exceptional virulence.

B. Development of vaccines against bacterial toxins.

C. Development of vaccines against highly pathogenic rickettsia.

D. Study of bacterial toxins

E. Cloning of bacterial toxin genes into foreign bacterial species.

F. Cloning of acetyl cholinesterase genes (nerve gas antidote)

G. Proposal to construct new high containment aerosol testing facility at Dugway proving grounds.

H. Existence of classified research projects at Fort Dietrich.

I. Apparent attempt to create the appearance of a "bioweapons gap" by the placement of inflammatory articles in the press.

J. Request to National Academy of Sciences for consultation on the potential applications of gene splicing to biological warfare.

The following comments relate to the United States. It is not at all unlikely that the USSR is engaged in similar activities; however, I am unaware of any reliable information. Items A-G above represent publically known DOD activities that are presented as purely defensive; in addition to the above argument that defense vs offense in this area is purely a matter of intent, there are a number of items for which it is difficult to make any argument in support of the defensive rationale.

In my view, the Army has failed to make a convincing case for the need to construct a new aerosol laboratory at Dugway proving grounds for purely defensive purposes. This view is shared by many scientists and was reported widely in the press earlier this year. My own views on the subject are summarized in two pre-trial depositions for a lawsuit to enjoin the construction of this facility brought by the Foundation on Economic Trends. These depositions are included here as Appendix A.

A more disturbing, if less definitive item, is the appearance in the Wall Street Journal and the Washington Post during early 1984 of a series of highly inflammatory articles purporting to show that the USSR is involved in an extensive program to develop new biological weapons by means of genetic engineering technology. The most inflammatory of these was a column by Jack Anderson in the Washington Post, Feb. 21, 1984, which is included here as Appendix B. One's suspicions as a scientist were aroused by a series of glaring errors and obvious fabrications in this and the other articles.

The Anderson article was based on a "secret CIA document" which stated that the USSR had developed a remarkable new technology, involving "gene splicing techniques as ominous as the atom-splitting discoveries that led to the nuclear bomb". The technical name for this research is "recombinant DNA technology". "The Soviets have developed a process for for removing segments of DNA from the cells of one species and attaching them to that of another, thereby creating a new organism" and "the U.S. is dangerously far behind in developing biotech weapons"... The articles in the Wall Street Journal elaborate on this theme at great length, including allegations that the Soviets have transplanted the gene for cobra venom into influenza virus, to generate a super-germ, capable of wiping out millions by the flu-snake-bite combination. Anderson's article concludes that "the most promising defense against biological warfare will come from research in recombinant DNA technology".

The most disturbing thing about this and the other articles is that it strains one's credibility to the breaking point to imagine that the CIA was unaware of the gross factual errors contained in them. One is forced to conclude that the articles were planted and that they constitute an example of the now classical "missile gap" ploy in which a fictitious weapons technology gap is created in the mind of the public in order to soften the opposition to yet another escalation of the arms race. One might speculate further that the new

Dugway lab - which was publically announced soon after the appearance of these articles - could well have been the objective of this ploy.

One could question the defensive justification of the other items at some length as well; I believe that this is unnecessary here and I would conclude by saying that I believe there are grounds for concern over the possibility that the US and perhaps also the USSR are about to initiate research into offensive biological weapons, based on allegations that the other side is doing so and there is no choice. My final comment is that President Nixon was entirely correct in his assessment that biological weapons are not a credible threat to US security (or to USSR security) and that it is of no direct concern to either power what the other is doing in this area. Rather, the development of biological weapons, with or without gene splicing, should be of concern to smaller nations, particularly those of the third world, who could be the object of covert attacks by either of the major powers. Unfortunately, all nations, great and small, may have to worry about the use of biological weapons by terrorists.

AP[illegible]

DECLARATION OF RICHARD P. NOVICK

RICHARD P. NOVICK declares:

1. I reside at 10 West 86th Street, New York, N. Y. 10128

2. I am a micro-and molecular biologist and a medical doctor. Attached is my curriculum vitae with the same effect as though fully set forth herein.

3. In summary, there is very serious concern for the safety of local workers and the general public in connection with the testing of aerosols containing lethal microorganisms, even in a facility with the best possible safety features. These concerns are outlined in the following paragraphs.

4. As a former member of the National Institutes of Health Recombinant DNA Advisory Committee and as a microbiologist with a special interest in infectious diseases, I am familiar with the problems of containment of highly pathogenic organisms. In formulating the NIH Guidelines for research with recombinant DNA, we realized that absolute containment is a theoretical as well as a practical impossibility and for this reason, developed the concept of biological containment. Here, the potentially dangerous material is contained within an organism that is genetically crippled and therefore unable to survive in the environment. This strategem would obviously be unavailable to the Dugway facility since its purpose is necessarily the opposite.

5. Additionally, certain types of experiments were forbidden because they were potentially too dangerous even under the most

stringent conditions of physical and biological containment. As a corollary of this concept, it is notable that there were numerous accidents and not a few deaths in the original high containment (equivalent to P4 or BL4) facility at Fort Dietrich prior to 1969 when biological weapons research was essentially terminated at that facility following President Nixon's directive. It is additionally noteworthy that laboratory workers are always immunized against dangerous pathogens that they are handling, even if the work is done at the highest level of physical containment.

6. A further concern relates to the testing of aerosols containing the most lethal agents known - which is reportedly the primary purpose of the new facility at Dugway. Aerosols are the most dangerous vehicle for dissemination and the most difficult to contain; the NIH Guidelines are focussed on the absolute avoidance of aerosols.

7. An entirely effective and much safer alternative would be to use simulants. The characteristics of aerosols are based on such physical properties as particle size, nature of the suspending medium, etc.; therefore, the aerosol characteristics of pathogens can be simulated with complete assurance by non-pathogenic organisms of the same general types. Indeed, the purpose of developing defensive equipment is much better served by the use of simulants that are more resistant to inactivation by environmental agencies such as ultraviolet radiation, drying, oxidation, etc. than the pathogenic organisms of concern, than by the use of the pathogens, themselves.

8. There is, in conclusion, no scientific justification for the construction and use of the proposed high containment laboratory at Dugway in connection with the development of defensive biowar measures.

I declare under penalty of perjury that the foregoing is true and correct.

Richard P. Novick

Dated: December 14, 1984
New York, N.Y.

RESPONSE TO ENVIRONMENTAL ASSESSMENT OF PROPOSED DUGWAY BIOWAR LABORATORY

By Richard P. Novick, M.D., Director, the Public Health Research Institute of the City of New York, inc.

1. I am the same Richard P. Novick that filed a deposition with the original lawsuit to which this Environmental Assessment is a response.

2. The Environmental Assessment is summarized for the purpose of discussion in the following paragraphs, A-D.

A. Purpose and need. As quoted by Environmental Assessment, Army Regulation 70-71 directs defense material to be effective against "all the general classes of microorganisms and toxins that can be used as biological warfare agents". DPG facility is intended to:

a) test [defensive] equipment;

b) fill knowledge gaps with respect to the "biological threat";

c) conduct tests with pathogens requiring stringent containment;

d) carry out DPG mission.

Overall: develop capability to warn and protect US personnel against biological attack. Danger of a Soviet attack is "very real."

B. Types of procedure:

i) Aerosol challenges of detection and protection devices.

ii) Aerosol tests to monitor contamination/decontamination

iii) Tests of detectors and alarms with aerosol challenge.

iv) Development of methods of aerosol analysis.

C. Alternatives to BL4 aerosol lab:

1) Use simulants

2) Construct BL4 lab elsewhere

3) Use Fort Dietrich

4) Use existing facilities (BL3) at DPG

2) and 3) are equivalent to BL4 lab at DPG and require no separate consideration.

1) and 4) are in effect two sides of the same coin.

The main question is that of whether simulants would satisfy the requirements for the development of defensive and detection devices.

D. Simulants are claimed to be inadequate because
efficacy of testing program
requires evaluation with "threat agent", as follows:

a) Tests with "threat agent" must be performed to verify detector sensitivity;

b) Tests with "threat agent" must be performed to evaluate penetrability of protective equipment;

c) Decontamination tests must be performed with "threat agent";

d) Data on persistence and resistance to environmental influences cannot be obtained with simulants;

e) Data on infectivity, symptomatology and lethality cannot be obtained with simulants.

3. These points do not constitute a defensible case for rejecting the exclusive use of simulants for the stated purposes ("a-e" refer to the immediately foregoing points):

a) and b): Development of defensive and detection equipment can be performed with absolute confidence and with absolute safety by the use of killed organisms. These will have precisely the same particle size and chemical composition as the live organism and no containment would be necessary; indeed, field conditions could be much better approximated by performing the tests outdoors.

c) and d): Decontamination analysis and tests of persistence do not require aerosols; additionally, these tests can be performed in complete safety by the use of live attenuated organisms such as those used for vaccines; it is noteworthy that if the vaccine strain of anthrax had been used by the British, Guignard Island would be inhabitable rather than closed to humans for 200 years because of the contamination with virulent anthrax spores. Prudence would suggest that extensive tests with vaccine strains be done with moderate containment; however, these tests would certainly not require a BL4 laboratory.

Susceptibility testing can also be done with attenuated strains; however, it seems difficult to justify such testing as having anything to do with defense - if there has been an attack, the attacked area will be closed until it has been determined to be safe. This will require direct examination for live organisms and prior knowledge of the organism's susceptibility to environmental factors will be of little or no use. It is argued, additionally, that if there is no vaccine strain for any of the organisms regarded as a "threat agent", one would be well advised to develop such a strain as soon as possible.

e) Applicable new data on "infectivity, symptomatology and lethality" cannot be obtained, with or without a BL4 laboratory, since experiments with live human subjects would not be permissible and animal models are inadequate. "Symptomatology" is well known for most of the agents under consideration on the basis of natural disease and experiments performed by the Japanese during World War II on human subjects. "Infectivity" and "lethality" data are not required for defensive purposes, in any case.

These considerations apply to live organisms. With respect to toxins, since these are non-infectious and will not persist in the environment, high containment levels would not be required. Safety precautions for the protection of workers would be required and these are obvious enough.

4. These considerations convince me that any research into biological warfare agents required for defensive purposes can be performed with full confidence and reliability without any special containment. It should be remembered that all offensive and defensive research with hydrogen bombs is performed with simulants since these weapons cannot be tested nor can defensive equipment be evaluated by challenge.

5. Certain items in the Environmental Assessment are particularly prone to raise suspicion of offensive intent, in violation of the biological and Toxin Weapons Convention. In particular, further analysis of the infectivity and lethality of a potential agent would be unnecessary for any imaginable purely defensive purpose. The infectious characteristics

of most of the "standard" agents are very well known, and, in the event of an attack, the remedial measures required are obvious enough without any additional data of this type. Additionally, the filling of "knowledge gaps", suggested to be an important part of the program, arouses strong suspicion that new types of agents will be developed and tested for their potential as bioweapons. A similar argument can be made for the proposal to gather information on the susceptibility of biological agents to battlefield conditions. Knowledge of such susceptibility can be useful only in connection with the development and testing of potential bioweapons.

6. It has been reported in the media that the USSR is actively developing new bioweapons by means of recombinant DNA technology and this claim has been echoed by Secretary Weinberger as a rationale for stepped up defensive biowar research such as that proposed for the DPG laboratory, implying that the US would have to initiate research of the same type in order to counteract this Soviet initiative.

This argument has been used to justify anticipatory research into the types of bioweapons that such an adversary might be expected to develop. Although any interest in such research has been vigorously denied by the Defense Department, one suspects nevertheless that the types of research that were noted above as lacking any defensive justification are aimed in this direction. It must be emphasized, however, that anticipatory research into potential bioweapons, involving the development of novel types of agents, with or without recombinant DNA technology, is an exercise in futility. There is an infinite number of possibilities for any given organism and there is no possible way to anticipate or predict what any potential adversary may be doing. *No modification by recombinant DNA technology of microorganisms that could be used as bioweapons can be justified as defensive research. Any such research is prima facie evidence of offensive intent.* Finally, it must be realized that pathogenic microorganisms are of little use as weapons in open warfare. They are highly unreliable, difficult to control, and unlikely to be effective. It is, in fact, unthinkable that an adversary such as the USSR would use them in open combat, violating international treaties, evoking universal revulsion, and risking nuclear retaliation. Much more likely is their potential as covert weapons that could be used surreptitiously to undermine a smaller nation under circumstances where overt military action is is not an acceptable option. In such circumstances, it would be essential to avoid detection; thus a flagrantly gene-spliced organism - such as influenza virus armed with cobra venom (which the Soviets have been accused of developing) - could never be used because its origin would be obvious. Rather, one would have to use an agent that could plausibly occur naturally in the region under attack. Recombinant DNA or other genetic technology could be used, for example, to modify the immunological properties of an existing agent so that the enemy population would be uniformly susceptible while friendly elements could be immunized. It is, incidentally, most unlikely that the pathogenicity of any natural organism could be "improved" by genetic manipulation and there are no realistic grounds for concern on this score. In other words, no conceivable Soviet biological weapons program could constitute any direct threat to the security of the US. Biological weapons development by either side would have to be viewed as threatening to smaller nations, especially those of the Third World.

Mr. Wyden. Doctor, we thank you and thank our other panel members for their participation. The gentleman from Minnesota?

Mr. Sikorski. I thank the Chairman. I would like to follow up Dr. Novick with an area of concern that you have outlined. The chairman has for some time, because of the jurisdiction of this committee and his longstanding concerns in the area, has focused on this before.

You were somewhat prophetic back over 10 years ago at the Asilomar Conference where you recognized the potential contribution that genetic engineering could make to biological weapons and warfare.

Can you briefly view those concerns?

Mr. Novick. My concerns about the utility of, let's say, modern biology for weapons development goes back somewhat earlier than the Asilomar Conference. It is because I have been working with Staphylococcus aureus which produces enterotoxins which have been of some interest to the military for many years. My interest was aroused back in the sixties when I was invited to initiate research by the Defense Department in that area.

Ever since then I have been concerned about the misuse of my own particular type of research. The concern at Asilomar was primarily with the idea that you could introduce a dreadful item such as botulin toxin into the common coli bacterium and perhaps contaminate water supplies with that and so forth. As time has gone on, my feeling is that that is less of a concern than it might have been because I don't believe it would work. Our concern has evolved since then to more sophisticated items such as the one I mentioned where one could modify the immunological properties of an agent to enable it to escape detection or to bypass the defenses of a target population.

I would also add that in my own personal view one is not likely to be able, or even need, to create an organism that is more pathogenic or more deadly than what is out there. There are plenty of deadly bugs out there you could use if you want. One might be more interested in modifying existing pathogenic to make them more useful than in creating anything more deadly.

Mr. Sikorski. More sophisticated. Would it be fair to say your general concerns remain, your specific concerns have now evolved with the evolution in biotechnology to embrace or to ferret even more sophisticated, more deadly kinds of warfare?

Mr. Novick. I agree with that assessment.

Mr. Sikorski. This committee and subcommittee have jurisdiction over the entire production of nuclear weaponry and has under the leadership of the chairman looked at the incredibly inept, at some points, security that surrounds that. The concerns you raise and the interest of the military in this has to even more engage our concern because of the same kind of security in this area would take.

At the Asilomar Conference over 10 years ago, the participants—scientists who were there—did not embrace opposition to this biological warfare. They were reluctant to embrace full opposition. Is that still the case?

Mr. Novick. I think that the official position of scientific bodies such as the Asilomar group and the Recombinant DNA Advisory

Committee, would wish only to deal with laboratory safety, which extends now to the environment, to some extent. These groups did not wish to take on any political issue such as the question of utility for biological weapons.

To be quite frank about it, I think there was fear at the time of the Asilomar that if the group were to adopt a strong statement biological weapons, it might arouse even greater fears in the public vis-a-vis the technologies that were then extant. Therefore, they felt discretion was the better part of valor.

Mr. SIKORSKI. Is it discretion and valor alone? Some have suggested that it derives from a concern over funding as well. After all, the military is—and we have seen over the last few years an accelerated funding source of biotechnology or biotechnological research. Is that part of the concern as well?

Mr. NOVICK. I believe at the time of Asilomar it was more a matter of discretion. At present, with draconian budgetary cuts hovering over us, I think that is true. Scientists are now much more concerned about their funding sources, and would be more reluctant to voice public opposition. I think some of my colleagues certainly are considering Defense Department funding.

My own personal view is that it is a pity the Defense Department should be engaged in supporting research in the private sector because I believe that carries with it certain potential consequences which would be best avoided. I would prefer that the money go through the NIH even for the same projects if possible.

Mr. WYDEN. Would my friend yield briefly on this point? I want to make sure I understand this. The Department of Defense pre-Asilomar asked you to do some basic research in this area, and you, for the reasons you outline in your testimony, said that you would not do that. Is it my understanding that they asked you again most recently?

I don't want to intrude on the gentleman's time, but I would be very interested in hearing a description of what you were asked to do, and what your response was, and when that took place.

Mr. NOVICK. It was about a year ago, that I received a packet in the mail inviting a request for proposal. This was a form which they sent to me, and probably other people as well and the request was to outline a project along certain lines involving research on Staphylococcus aureus enterotoxins, which were very much a part of our work at the time and still are.

I didn't quite know how to handle it. I elected not to respond. I would be happy to make it available if you wish.

Mr. WYDEN. I think there would be interest in that. We will hold the record open. I thank the gentleman.

Mr. SIKORSKI. I thank the chairman for helping out in that area. Then as I understand the situation, just in summary, you have an instance where there is a lot of money coming throughout military funding sources. At the same time—which makes the military funding loom even larger—is insufficient funding through NSF and NIH in this area. So the dependence is growing on the military funding source and there is subsequently perhaps a softening of the concerns in the scientific community over this whole issue of biologic warfare activities. Is that a fair assessment?

Mr. **Novick**. As institute director, I have to be very careful about the funding potential of the people working in the institute. One of my staff came to me the other day and asked how I would feel about his going after a military contract. I sort of gulped and said, I can't stop you from applying for it. I hope we can defend it as not involving biological warfare. And for myself, I would not have done it, but I couldn't really stop him from doing it because he in fact had lost his grant, and was very much up against the wall as far as funding was concerned.

Mr. **Sikorski**. It is a question of whether we are going to lose a mind in this effort or an effort in this area that is important.

Mr. **Novick**. I would have thought so.

Mr. **Sikorski**. Mr. Lappé.

Mr. **Lappé**. I just wanted to add my research indicates that vast preponderance of work that has taken place to date on vaccine development has been funded by the military. I also, along with Dr. Novick, note the irony of this and the potential bifurcated uses of some of this research. I would very much prefer to see this work sponsored by NIH.

Mr. **Sikorski**. I share your concern. Thank you, and I thank the chairman.

Mr. **Wyden**. Thank the gentleman. Dr. Novick, in your testimony you mentioned the developments in biological sciences make biological weapons available to terrorists. The subcommittee has often been told great intellectual capacity is needed to manipulate organisms genetically, but the equipment needed to grow organisms may be minimal; is that correct?

If so perhaps you can elaborate.

Mr. **Novick**. The actual physical equipment is certainly minimal. You can do it in your bathroom if you wish. But what I think may be a deterrent is two things. First of all, it is not easy to get a hold of the nastiest organisms. That is, you could not obtain them from a type culture collection without a university affiliation of some sort. It is possible, but it would take a fairly clever person to do it.

The other thing is that if you are trying to handle organisms like this, you have to know what you are doing. You can't just take Bacillus anthracis, for example, and grow it up in your bathroom because you would get anthrax for sure if you didn't know what you were doing. They are very dangerous to handle .

While it is true that it doesn't take elaborate equipment, it at least takes microbiological sophistication to handle deadly organisms. I also would argue that as far as terrorists are concerned rDNA doesn't offer very much. They could do well enough with the common garden variety if they wish. Hopefully they won't.

Mr. **Wyden**. That is certainly all our hope. There is on question the possibility of terrorism is frightening to all Americans, but we are also concerned about military R&D and the potential of biologic weapons overtly and covertly in the environment should keep us alert to unintended hazards from more peaceful sources as well.

Do you think the potential for biological weapons may reflect the possible hazard in other environmental releases of genetically manipulated organisms?

Mr. **Novick**. My primary view has always been that the most serious possible hazard with recombinant organisms was the intentional one of creating novel pathogens, either for the purpose of making a weapon or even for research.

One originally, if you recall, had a series of experiments that were prohibited by the NIH guidelines. These involved primarily the cloning of the most potent toxins into other bacteria. The experiments were prohibited because they were thought to be very dangerous, even though they might have been done without the intention of making weapons. As far as I know, the potential hazards of the organisms that might get released into the environment would be inadvertent and are not foreseeable in the same sense that the cloned toxins are foreseeable.

Mr. **Wyden**. Let me turn to one other area. This is the area of the Geneva Summit and the Congress has been very assertive in trying to make the case for clear arms control policy and that policy up to this point has dealt almost exclusively with nuclear weapons, defenses against nuclear weapons. Do you think that there has been sufficient attention paid to biological weapons and how advances in biological sciences have increased the likelihood of biological warfare?

Mr. **Novick**. I think generally the official position around the world is that the 1972 convention adequately covers all possible misuse of biological research for warfare, and I think therefore it has been kept out of the public eye and out of disarmament conferences and so forth. I don't totally agree with that. I think that, as I said, there is room for a lot of creative interpretation of the wording of that treaty, and I personally would like to see it be strengthened with the express prohibition that I mentioned before, and with a verification provision added.

While I certainly think a nuclear holocaust is much more scary than a biological attack, I am not comfortable about that in the future.

Mr. **Wyden**. You also reviewed in your testimony the new capacity and new interest in biological weapons and suggested that there is new military research and development among biological weapons. I think what we would be interested in knowing whether it is correct that on new R&D offensive or defensive by any country, how that would affect the ability to achieve arms control?

Mr. **Novick**. Well, as I suggested in my comments, there was a series of unpleasant articles in the press last year and those, I feel, served to fuel a lot of concern in military circles and may have been planted there for that purpose.

Secretary Weinberger in his defense of the Dugway Laboratory alluded to this information and said that this was one of our concerns, that the Russians were doing this and we had to do the same, and that the facility would not foreswear using recombinant DNA organisms in its testing.

So while in the information that was publicly available about the Dugway facility at the time, it was clearly stated that there were no plans to use recombinant DNA, they nevertheless would not say there never would be such plans.

Mr. **Wyden**. Well, a few years ago the Congress required the Department of Defense and all other departments prepare for the Arms Control and Disarmament Agency an arms control compact statement on any program that might affect U.S. arms control policy.

Now do you know if an arms control compact statement has been prepared on any of the research and development activities that you have described?

Mr. NOVICK. I am not really aware of any that have, I am sorry to say.

Mr. WYDEN. Well, I think it is pretty clear that new R&D by any country could effect the ability to achieve effective arms control and I suspect it would be useful for this subcommittee to inquire from the Committees on Armed Services and on Foreign Affairs if that requirement for an arms control compact statement has been followed for biotechnology research and if so, for which products.

Our review of the nonclassified text of fiscal year 1986, the arms control compact statements printed by the Foreign Affairs Committee, it appears that there are no biological projections mentioned and thus, no information on biotechnology presented in the arms control and disarmament agency.

It is my view, and I know this is felt strongly by Chairman Dingell, that U.S. arms control policy should reflect developments in the sciences in this area and I think without objection, let us put section 36 of the Arms Control and Disarmament Act in the record and the subcommittee will pursue this.

[The excerpt referred to follows:]

ARMS CONTROL IMPACT INFORMATION AND ANALYSIS

SEC. 36.[35] (a) In order to assist the Director in the performance of his duties with respect to arms control and disarmament policy and negotiations, any Government agency preparing any legislative or budgetary proposal for—

(1) any program of research, development, testing, engineering, construction, deployment, or modernization with respect to nuclear armaments, nuclear implements of war, military facilities or military vehicles designed or intended primarily for the delivery of nuclear weapons,

(2) any program of research development, testing, engineering, construction, deployment, or modernization with respect to armaments, ammunition, implements of war, or military facilities having—

(A) an estimated total program cost in excess of $250,000,000, or

(B) an estimated annual program cost in excess of $50,000,000, or

(3) any other program involving technology with potential military application or weapons systems [36] which such Government agency or the Director believes may have a significant impact on arms control and disarmament policy or negotiations,

shall, on a continuing basis, provide the Director with full and timely access to detailed information, in accordance with the procedures established pursuant to section 35 of this Act, with respect to the nature, scope, and purpose of such proposal.

(b)(1) The Director, as he deems appropriate, shall assess and analyze each program described in subsection (a) with respect to its impact on arms control and disarmament policy and negotiations, and shall advise and make recommendations, on the basis of such assessment and analysis, to the National Security Council, the Office of Management and Budget, and the Government agency proposing such program.

(2) [37] No request to the Congress for authorization or appropriations for—

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[35] 22 U.S.C. 2576. This section was added by sec. 146 of Public Law 94-141.

[36] Sec. 1(1) of Public Law 95-338 struck out the words "weapons systems or technology" and inserted "technology with potential military application or weapons systems". Senate Report No. 95-843, May 15, 1978, states at page 3 that this change was made "so that there would be no question that technology with potential military application, rather than, simply, weapons technology, could be reviewed and reported upon under the legislation."

[37] Sec. 1(2) of Public Law 95-338 amended and restated subsec. (b)(2) which previously read as follows: "(2) Any request to the Congress for authorization or appropriations for—"(A) any pro-

Continued

(A) any program described in subsection (a)(1) or (2), or

(B) any program described in subsection (a)(3) and found by the National Security Council, on the basis of the advice and recommendations received from the Director, to have a significant impact on arms control and disarmament policy or negotiations,

shall be transmitted without a complete statement analyzing the impact of such program, either as an individual program or as an aggregation of related programs, on arms control and disarmament policy and negotiations. Any such statement transmitted in classified form shall be accompanied by an unclassified version thereof.

(3) Upon the request of the Committee on Armed Services of the Senate or the House of Representatives, the Committee on Appropriations of the Senate or the House of Representatives, the Committee on Foreign Relations of the Senate, or the Committee on International Relations of the House of Representatives or the Joint Committee on Atomic Energy, the Director shall, after informing the Secretary of State, advise such committee on the arms control and disarmament implications of any program with respect to which a statement has been submitted to the Congress pursuant to paragraph (2).

(c) No court shall have any jurisdiction under any law to compel the performance of any requirement of this section or to review the adequacy of the performance of any such requirement on the part of any Government agency (including the Agency and the Director).

Mr. WYDEN. I want to recognize the gentleman from Minnesota again for additional questions he may have.

Mr. SIKORSKI. I thank the Chairman.

Mr. Nicholas, do you see in the biodegradation work area a role for the sort of firms who belong to the ABC and the IBA?

Mr. NICHOLAS. I think this panel and the preceding panel present a range of activities, commercial and noncommercial, that biotechnology can be used in.

Biodegradation presents a reasonable potential for companies who are members of the various trade associations, but as I have pointed out in my testimony, there are substantial impediments to the rapid development of this technology, including the regulatory uncertainty surrounding the use of genetically modified organisms in the environment.

Mr. SIKORSKI. They have to know there is a market out there.

Mr. NICHOLAS. That is correct.

Mr. SIKORSKI. They have to—before they commit millions, maybe hundreds of millions of dollars to the development of a successful commercially feasible process in this area—they have to know that they are going to be able to get through a regulatory process, not with ease, with real scrutiny, but with some sort of parameters that make their financial investments look reasonable, is that correct?

Mr. NICHOLAS. That is correct. It is really a twofold process.

One, will landfills be changed as the primary method for disposal so there will be an incentive to develop alternative technologies and then second, will the regulatory picture for genetic engineering organisms be substantially worked out, recognizing of course that there are many ways these organisms could be used apart from releasing them into the environment?

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gram described in subsection (a)(1) or (2), or "(B) any program described in subsection (a)(3) and found by the National Security Council, on the basis of the advice and recommendations received from the Director, to to have a significant impact on arms control and disarmament policy or negotiations, shall include a complete statement analyzing the impact of such program on arms control and disarmament policy and negotiations."

Mr. SIKORSKI. So the current regulations say what in this area, looking at last year's RCRA, the new Superfund and pending regulations?

Mr. NICHOLAS. With respect to the use of genetically modified organisms the administration has proposed a series of guidelines which they published last December for introductions into the environment. Those will probably be republished at the end of January, and hopefully there will be more guidance at that time with respect to what EPA, USDA, and NIH will do with respect to genetically modified organisms.

Mr. SIKORSKI. Genetically modified organisms are going to trigger a very lengthy review process under these proposed regulations, isn't that true?

Mr. NICHOLAS. Well, under existing statutes various agencies have taken different positions with respect to the kind of information that may or may not be required. Each agency at this point has determined that they will proceed on a case-by-case basis.

Mr. SIKORSKI. What is bothersome here is that it doesn't give the kind of finite universe that a potential investor or company needs in the area of micro-organisms that are currently found. The review process should arguably, at least hypothetically, be shorter than one where there is a genetically engineered substance.

Mr. NICHOLAS. That is correct. The current EPA process is moving in the direction to treat indigenous organisms that are removed from the environment, selectively bred, and returned, differently from organisms that are mutated, whether genetically or otherwise. This latter category of organisms will go through a review process similar to that used by EPA for other products within the jurisdiction of the Toxic Substances Control Act and FIFRA.

Mr. SIKORSKI. Looking at the attitudes of people at EPA and other Federal agencies that have jurisdiction over the approval of these, what is their attitude toward the degradation? Do they think it has merit, it has pluses or minuses?

Mr. NICHOLAS. I think the ORD people at EPA see benefits to these techniques, as do others, but one of the things that one clearly should divide is the use of micro-organisms, whether genetically engineered or not, which are used in contained vessels or at the end of pipelines as opposed to organisms that are released into the environment.

It is clear that the organisms that will be released into the environment will require a more thorough analysis and review, particularly of environmental fate, than organisms that are used in contained vessels. There still remains a lot of research to be undertaken to take some of the laboratory strains and make them effective degraders of hazardous waste, and I think with the new Superfund amendments there is a real impetus for that work to be undertaken.

Mr. SIKORSKI. There are a lot of spinoffs to biodegradation that have or potentially have positive results for society, aren't there?

Mr. NICHOLAS. Certainly. Now it is interesting I think that one of the things that the new Superfund money has the potential to do is to help answer some of the questions about what happens when organisms are used in the environment, and that may provide some of the answers to the regulatory questions that EPA and the other agencies are seeking to look at.

Mr. SIKORSKI. Some of that basic research we started the series of hearings with earlier this year.

Mr. NICHOLAS. That is correct.

Mr. SIKORSKI. I thank you.

Mr. Lappé.

Mr. LAPPÉ. One additional point. The obverse side of controlling biohazards is the generation of new hazards. There are a lot of naturally occurring degradation reactions occurring in the environment that generate very toxic materials. There are methane producing bacteria that will take chlorinated solvents and break them down to produce vinylchloride as the end point. One might want to look at ways in aggregate to regulate and control natural processes to make them less harmful as part of this overall view of biodegradation.

Mr. SIKORSKI. I thank you.

Thank you, Mr. Chairman.

Mr. WYDEN. I thank the gentleman.

Dr. Lappé, in terms of the agricultural advances that might be available to the developing world through biotechnology, I understand that you are an expert, for example, in what might be achieved through genetic engineering in this regard.

Could you elaborate further for the subcommittee?

Mr. LAPPÉ. I think that there is a two-tiered set of priorities for the developing world, only the second of which has to do with genetic engineering.

The first tier has to do with using recombinant DNA techniques to rescue, secure and otherwise protect the germ plasm of the wide variety of genetic strains that are part of the mainstay of the developing world, and ultimately the world base of gene stocks for food crops.

Second, recombinant DNA can indeed be used to transfer nitrogen fixing genes into organisms that will then cohabit with or infect plant cells and make them capable of fixing nitrogen. This is one of the real advantages to a world that is presently dependant on nitrogenous fertilizers.

Additional development that recombinant DNA has already been useful in has been to make some of the grains and cereal crops in the developing world more nutritive by providing variants rich in very deficient amino acids, like lysine or methionine, or tryptophan.

It is worth noting these developments are primarily intended to increase the value of these essential commodities as animal feedstuffs, and this drives against the logic of supplying a world that is needful of these proteins.

Mr. WYDEN. Without the help of the large firms, the large industrial firms, are there other ways that developing countries can get biotechnology for food directed to their needs or if we cannot get these large industrial firms involved, is the science and production just going to be beyond the capacity of the developing countries?

Mr. LAPPÉ. There is an effort under way under the UNIDO group from the United Nations to set up a two-pronged series of centers, one in Italy, one in India, that would address the real problems with recombinant DNA. Most of the outside observers like myself who have watched this process unfold are skeptical about its likely success. To answer your question directly, it is the large firms in this country and their multinational arrangements, particularly with companies in Japan, that really hold all the cards as to who will get benefits from rDNA research.

Mr. Wyden. Mr. Nicholas, just a couple of questions for you.

I think you know the subcommittee is very interested in the question of toxic chemicals, dioxin, PCB in the environment, and of course it is quite exciting to hear you tell us about developments that scientists have bacteria that can destroy these kind of chemicals.

I think what we would be interested in knowing is what you see the real potential for all this as a technique for cleaning up the toxic dump sites, particularly the sites that would be on the national priority list.

Mr. Nicholas. As I address more completely in my testimony, laboratory strains have been developed that can degrade some of the most toxic chemicals that many people have been concerned about. There are still significant problems in moving these strains to the marketplace, but I think there is a real potential there and it is going to take significant work.

Perhaps as these things can be done in contained vessels , we are going to see a more rapid use of these technologies. The demonstration provisions of the Superfund bill should clearly make this more easily undertaken.

Mr. Wyden. Where do you think the major application of biodegration are going to come?

Mr. Nicholas. First of all, they are probably going to come in the waste process itself where you have the well-characterized, frequently single or dual, constituent waste. At the present time, micro-organisms have been developed that can degrade individual substances but it is very difficult to get them at this point to degrade complex mixtures.

So one of the closer applications is probably going to be with respect to waste stream and waste processes, possibly also the ability to clean up ground water that has been contaminated and which is not easily accessible.

Mr. Wyden. Well, gentlemen, I don't have any further questions. Does the gentleman from Minnesota have any additional?

Mr. Sikorski. No. Thank you, Mr. Chairman.

Mr. Wyden. Let me recognize minority counsel.

Mr. Wilson. Thank you, Mr. Chairman.

I have a couple questions for the panel, the first one to Mr. Nicholas.

One question was raised this morning on whether patent laws are keeping up with biotechnology or whether it was merely an administrative hangup; that patent examiners are unable to process the numbers of patent applications.

From your perspective as an attorney, which do you think is the more likely explanation?

Mr. Nicholas. I don't think that either is unlikely. They are not mutually exclusive.

Shortly after I left the Science and Technology Committee, I undertook some work for the Office of Technology Assessment. One of the questions I looked at was, to what extent are the patent laws not keeping pace with the developments in molecular biology.

There was speculation on the part of companies as to how they were or were not going to be protected, but I think most of that reflected the uncertainty of how the patent office would treat the various applications. As with any new technology, there is a sorting-out process. It is very difficult at this point to get a real feel for how well patent law will protect the technology.

As I understand it, the Office of Technology Assessment has been requested by several Members of Congress to undertake a review of the patent area, and if they decide to do that, it probably will commence some time in the near future.

Mr. WILSON. A question of Dr. Lappé. If certain products have clear benefits but are comercially unprofitable, as you testified, do you think it advisable for the Federal Government or others to pay for development, marketing, distribution, and insurance against possible adverse consequences for those products?

Mr. LAPPÉ. Beginning with the latter point, I think that it is very appropriate for the Federal Government, as it has taken with some of its vaccine programs, to underwrite or at least provide the premiums for liability insurance for developing essential commodities that might pose inadvertent risk.

As to whether the lion's share of the complete mix of product development should be funded by the Government, my tendency is to see and encourage a lot more than that. The Government could, by offering proper incentives, as it does under the Orphan Drug Act, encourage industries in those directions without subverting the full industrial base for their development.

Mr. WILSON. Dr. Novick, a couple of questions. Do you believe that in the face of the rapid development of biotechnological techniques that we have heard about, and their applications, and our knowledge that the Soviet Union and others are at least aware of these developments, and your own statement in the testimony that it is only a matter of time until terrorists hit upon the use of biological weapons—whether or not those weapons involve recombinant DNA—that we should ignore the possibility of defending against biological weapons?

Mr. NOVICK. I am not advocating ignoring the possibility. I am sort of throwing up my hands in despair as far as any real defense can be conceived of.

If you happen to have advance knowledge of what bug they are going to use, then you can go and vaccinate everybody. But if you don't, if there are, say, 5,000 different possible agents, you can't imagine vaccinating a large segment of the population against it.

I think we are helpless against a determined, effective use of a biological agent. I think what we are really dependent upon, and fortunately, so far, I think it has worked, is that the world takes a very dim view of any such activity and I think will continue to do so. This will not deter terrorists, unfortunately.

I hope there are people who are cleverer than I and can imagine a way of protecting whatever population may be subject to terrorist attack against biological weapons. I have no way of knowing how to do it.

Mr. **Wilson**. Is it your testimony that as far as you know we are helpless against terrorist threats to use bio-weapons?

Mr. **Novick**. I think we would be helpless. I do think, however, that a country like this—a country with a well-defined water supply, good sanitary measures, and good public health measures—is much safer than a less well-developed country where water supply could be ruined very quickly. I think the water supply is the most likely place where one would go with this sort of thing.

Mr. **Wilson**. I only have one more question.

In March, the subcommittee heard testimony that the National Institutes of Health lacked an aggressive, well-funded program for vaccine development. Your testimony today indicated that you know of no way to draw a line between offensive and defensive or humanitarian use of vaccines.

Do you believe U.S. military forces ought not to have vaccines against dysentery and other diseases if the Department of Defense or the National Institutes of Health can develop them?

Mr. **Novick**. I think there ought to be vaccines against every imaginable pathogen.

What concerns me is that there are diseases that affect very, very large numbers of people against which the Army is not preparing vaccines. On the other hand, there are other diseases that affect very small numbers and are very deadly and don't really pose a threat to U.S. troops in the field and against which the Army is very interested in making vaccines.

So it is a matter of emphasis and of subtle interpretations that lead to my concern, not the global idea of whether or not there should be vaccines, which, of course, there should be. As I said before, I think they should be done in the public sector openly and with full knowledge of everyone concerned.

Mr. **Wilson**. So your concern, as I understand it, is if they are developing vaccines against something that you consider to be a widespread threat, that is OK; but if they are developing a vaccine against something that doesn't affect as many people, you are concerned.

Mr. **Novick**. Yes. It is not that I am concerned with developing the vaccine; I think the vaccine should be developed. My concern is where the priorities are and why those priorities are being picked.

As I said, in an area where there is much more heat than light, one has to make interpretations based on what knowledge one has. My interpretation of that is one of suspicion—let's put it that way—rather than any real knowledge.

Mr. **Wilson**. So you would see the development of vaccines as evidence that a more concentrated research effort may be going on in biological warfare. idence.

Mr. **Novick**. It raises my concern in that area.

Mr. **Wilson**. I have no further questions.

Thank you, Mr. Chairman.

Mr. **Wyden**. Thank you.

I want to touch on one other point. Dr. Novick, would it be fair to say an additional concern that you have in this regard is that there be disclosure of what is done in the civilian sector and what you are concerned about is covert activity in the military sector. Is that a fair appraisal of your concern in this area?

Mr. NOVICK. Absolutely. May I just add one more point?

Mr. WYDEN. Before you do, I didn't want our minority counsel to think I was gavelling him down.

Did you get a chance to ask all of the questions you wished to pursue?

Mr. WILSON. I have, Mr. Chairman. Thank you.

Mr. NOVICK. I wanted to add one more point to the question of why the Army was interested in my doing research in enterotoxins. They, as you know, are the cause of food poisoning and certainly the mess hall is a very good place for food poisoning to occur.

On the other hand, the research that I would be doing really wouldn't have any impact on food poisoning. That has to be dealt with by careful handling and preparation of food. And the enterotoxins are widely regarded as very good as incapacitating agents. If you have ever had food poisoning by staphylococcus, you know what I mean. The concern here is development of incapacitating agents for potential use in warfare.

Mr. WYDEN. No further questions from the minority.

If you all don't have further comments, we will excuse you and thank you again for a very helpful presentation.

The subcommittee will reconvene at 2 p.m., where we will have witnesses from Government agencies and discussing regulatory matters, and we stand in recess until 2 p.m.

[Whereupon, at 12:45 p.m., the subcommittee recessed, to reconvene at 2 p.m., this same day.]

AFTER RECESS

Mr. WYDEN. The subcommittee will come to order.

Our third panel, Dr. David T. Kingsbury, Assistant Director, Biological, Behavioral, and Social Sciences, National Science Foundation, Washington, DC, and I understand Dr. Kingsbury will be accompanied by Dr. John A. Moore, Assistant Administrator for Pesticides and Toxic Substances for the Environmental Protection Agency in Washington.

Gentlemen, we thank you for your participation today. I think you are all aware it is a tradition of this subcommittee to swear all witnesses, all witnesses before the subcommittee have right to counsel. I note you all have a copy of the committee rules with you at the table for your appearance. Do either of you gentlemen have an objection to being sworn as witnesses this afternoon?

Mr. KINGSBURY. No.

[Witnesses sworn.]

Mr. WYDEN. Gentlemen, we will make a copy of your prepared remarks a part of our hearing record in their entirety, and if you could summarize your principal concerns in the interest of time, that will allow plenty of opportunity for questions. Why don't we begin with you, Dr. Kingsbury.

TESTIMONY OF DAVID T. KINGSBURY, ASSISTANT DIRECTOR, BIOLOGICAL, BEHAVIORAL, AND SOCIAL SCIENCES, NATIONAL SCIENCE FOUNDATION; AND JOHN A. MOORE, ASSISTANT ADMINISTRATOR FOR PESTICIDES AND TOXIC SUBSTANCES, ENVIRONMENTAL PROTECTION AGENCY

Mr. KINGSBURY. Thank you, Mr. Chairman.

Mr. Chairman, members, and staff of the subcommittee, I am David T. Kingsbury, the Assistant Director for Biological, Behavioral, and Social Sciences of the National Science Foundation. I am here today in the multiple roles of working Chairman of the White House Domestic Policy Council Working Group on Biotechnology, and more importantly for the purpose of these proceedings as the first Chairman of the Biotechnology Science Coordinating Committee [BSCC] of the Federal Coordinating Council for Science, Engineering and Technology [FCCSET].

I would like to begin this testimony by providing the committee with a brief historical overview of the development of the Domestic Policy Council Working Group's activities and the development of the BSCC. I would then like to discuss the activities of the BSCC and finally to proceed to discuss some of the conclusions and questions which arose from a recent NSF/OTA workshop.

This workshop, which arose partially out of a request from this committee, was important because it was the first in a series of research-topic-oriented workshops intended to explore release of genetically altered organisms and their fate in the environment. I had the pleasure of serving as the chairman of the scientific sessions of the workshop which was entitled "Genetic Stability and Horizontal Transfer Associated with Deliberate Release of Genetically Engineered Organisms."

As Dr. Bernadine Healy described to this committee, in April 1984, a biotechnology working group was formed under the auspices of the White House Cabinet Council on Natural Resources and the Environment. The working group's activities included the international harmonization of our regulatory policies, questions of Federal support of research related to biotechnology, and the eventual commercialization of the findings of this research.

As we described to this subcommittee approximately one year ago, the working group focused primarily on questions related to regulation of biotechnology and the initial product was the December 31, 1984, publication in the Federal Register, of a proposed framework for biotechnology.

The public was invited to provide comments regarding all parts of this proposed coordinated framework, and many letters were received. A few details of the responses may be found in a recent Federal Register notice, published on November 14, 1985. The working group has examined these public comments carefully and the individual agencies are modifying their policy statements to reflect the positive and useful suggestions contained in those comments. The revised agency policy statements will be published in the Federal Register on approximately January 31, 1986.

In light of these concerns, the working group considered many alternative models as modifications or replacements of the proposed BSB. There remained consensus that interagency coordination of science questions resulting from applications of all types was desirable. However, there was also a consensus that there was no need for a second level advisory committee review.

The working group agreed that a committee made up of officials from NIH, NSF, EPA, FDA, and USDA could serve the required function and provide a forum for the exchange of information between these and other agencies as well as the public. Such a committee would include only Federal officials; therefore, scientific data contained in applications could be shared since confidential business information or other proprietary data could be appropriately protected. A coordinating committee of this type could also hold public meetings at regular intervals.

Following the decision to establish such a committee, its appropriate location was examined. HHS had been suggested for the BSB; however, several factors suggested that other locations should be considered. HHS contains within it two groups that would be members of the coordinating committee: NIH and FDA. Maintaining the committee within HHS might suggest an HHS point of view and open the question of rivalry between the new committee and the NIH RAC.

After all of the factors were considered, the working group felt that a location away from any of the agencies directly involved would be the most appropriate, and the Office of Science and Technology Policy was selected.

The Federal Coordinating Council for Science, Engineering and Technology [FCCSET] appeared to be a suitable organizational location and structure under which to place the functions of the coordinating committee. Accordingly a FCCSET committee was established to coordinate science issues related to research and commercial applications of biotechnology. The committee is called the Biotechnology Science Coordinating Committee [BSCC].

The purpose of the BSCC is to serve as a coordinating forum for addressing scientific problems, sharing information, and developing consensus; promote consistency in the development of Federal agencies' review procedures and assessments; facilitate continuing cooperation among Federal agencies on emerging scientific issues; and identify gaps in scientific knowledge.

The BSCC charter provides for the sharing of scientific information and authorizes the BSCC to seek and obtain all materials relevant to the details of an application and its handling by the agency. The BSCC is empowered to have periodic public meetings and to convene workshops, symposia, and coordinate special studies related to scientific issues in biotechnology.

The charter calls for the BSCC to be chaired by the Assistant Director for Biological, Behavioral, and Social Sciences of the National Science Foundation and the Director, National Institutes of Health on a rotating basis.

The BSCC has met and begun its work. The committee has scheduled meetings at approximately monthly intervals for the next several months and intends to continue this practice for at least the next 6 months. The first open public meeting is planned for February 14 and will be held in the auditorium at the National Academy of Sciences. I am very enthusiastic about the committee operations. Each member has clearly come with an attitude of open cooperation and mutual support. The discussions have been far-ranging and candid. While the committee does not have a mandate embedded in statute, each member has promised full participation through the signing of a memorandum of understanding which pledges full cooperation in the operations of the committee as set forth in the charter. The committee structure was approved by the Domestic Policy Council and has that council's support. This provides a basis of consensus at a very high level within the administration.

The committee has already been useful in providing assistance to one of the member agencies during the process of a product review, and there is no reason to anticipate that this close collaboration will not continue.

On November 21 and 22, 1985, the National Science Foundation and the Office of Technology Assessment cosponsored a workshop related to the horizontal transfer and stability of new genetic material introduced into the environment. The panel was composed of 18 scientists recognized for their expertise in ecology, plant biology, population biology, molecular biology, and related fields and included Government, university, and industry scientists. The workshop was open to invited outside observers, and over the period of the 2 days at least 40 observers from congressional staff, Government agencies, professional societies, environmental groups, and the press were present. It was a productive and stimulating meeting and represents the type of symposia and workshops of interest to the BSCC.

The goal of the meeting was to address a series of scientific questions related to the introduction of new genetic constructions into the environment. The discussion was relevant to both intentional and unintentional release of genetically modified organisms, although we focused on the intentional release question.

In previous scientific meetings dealing with questions related to intentional release of organisms into the environment, the scientific community had been reluctant to draw any generalizations regarding the effects of such introductions. Initially the NSF/OTA meeting was no exception, with the majority of the participants focusing on the gaps in our knowledge rather than on those areas where we have some understanding.

As the meeting developed throughout the first day, however, the amount of data sharing was considerable and the focus of the attention changed. By the second morning, the panel was willing to try to develop some generalizations which could be used to guide regulators and legislators alike. One factor dominated the discussions even when potential guidelines were being discussed: there was general agreement that, at the present time, each application must be judged on a case-by-case basis. However, there was also general agreement that not all intentional environmental releases would have the same potential impact.

It must be stressed that the workshop and this outline which resulted from it were not envisioned to be fully comprehensive but instead to focus on a limited number of questions about which we had some information. It is representative of the type of information currently available within the scientific community but which is generally not available in the form best suited for application to regulatory questions related to intentional releases of genetically manipulated organisms into the environment.

It was widely felt that nonsexual horizontal gene transfer betweeen genetically-modified and native plants was of such a low probability as to be negligible. The panel concluded that the only potential hazard posed by genetically modified plants was from the environmental effects of the new gene product itself and not from the fact that recombinant DNA technology may have been used to derive the new plant variety.

With genetically modified micro-organisms, the situation is somewhat different. Therefore, it is essential to identify the potential targets of a transfer which could possibly lead to undesirable effects and then to analyze the possible countermeasures that may be used. It was agreed that the existing technologies within modern molecular biology have provided for extremely effective countermeasures for many applications.

The net result is that the reviewing regulator must balance the mathematical probability of a transfer event with the mathematical probability of favorable environmental and selective conditions. In so doing, we will reach the boundaries of our knowledge, but is also likely that many of the envisioned applications will easily fall within those boundaries and can be examined confidently within our present body of knowledge.

During the workshop, a group of NSF program officers established a list of scientific priorities that might be studied in the future. This list is in my written testimony, and I won't read it here at this time.

I came away from the workshop with two concerns regarding the debate over the intentional release of modified organisms. First, it appears that many people view genes as infectious agents which, if given a chance, will spread throughout the environment infecting a wide variety of organisms. We know, of course, that this is not true. Genes are simply fragments of DNA which must be within a living cell in order to be duplicated and that once within that cell will most likely stay there.

Second, it is not uncommon for people to view micro-organisms in the environment as simply the wild brethren of our laboratory subjects. We view them as happy and well fed, waiting to take advantage of any and all new opportunities. In reality, life is much more difficult. Soil organisms, for example, divide on the average of twice per year and survive in a state of constant starvation. They are not physiologically well prepared to accept or incorporate new genetic material even if it would provide them a new capacity for growth. If the incorporation of that new gene involved production of a nonessential product, such as a pesticide, it is even less likely to ever occur.

We view this workshop as the first of a series devoted to specific areas of the broad topic of the environmental release of genetically modified organisms. At the pesent time, we have two additional workshops planned and have discussed additional meetings with the National Academy of Sciences and others.

Mr. Chairman, thank you for this opportunity to testify before the subcommittee. I would be delighted to answer any questions that you may have.

[Testimony resumes on p. 136.]

[The prepared statement of Mr. Kingsbury follows:]

STATEMENT OF DAVID T. KINGSBURY, ASSISTANT DIRECTOR, BIOLOGICAL, BEHAVIORAL AND SOCIAL SCIENCES, NATIONAL SCIENCE FOUNDATION

Mr. Chairman, Members, and Staff of the Subcommittee:

I am David T. Kingsbury, the Assistant Director for Biological, Behavioral, and Social Sciences of the National Science Foundation. I am here today in the multiple roles of working Chairman of the White House Domestic Policy Council Working Group on Biotechnology, and more importantly for the purpose of these proceedings as the first Chairman of the Biotechnology Science Coordinating Committee (BSCC) of the Federal Coordinating Council for Science, Engineering and Technology (FCCSET).

I would like to begin this testimony by providing the Committee with a brief historical overview of the development of the Domestic Policy Council Working Group's activities and the development of the BSCC. I would then like to discuss the activities of the BSCC and finally to proceed to discuss some of the conclusions and questions which arose from a recent NSF/OTA Workshop. This workshop, which arose partially out of a request from this Committee, was important because it was the first in a series of research-topic-oriented workshops intended to explore the current state of knowledge in subjects related to intentional release of genetically altered organisms and their fate in the environment. I had the pleasure of serving as the Chairman of the scientific sessions of the workshop which was entitled "Genetic Stability and Horizontal Transfer Associated with Deliberate Release of Genetically Engineered Organisms."

In response to a recognized need to carefully examine questions related to the regulation of biotechnology products, in April 1984, a Biotechnology Working Group was formed under the auspices of the White House Cabinet Council on Natural Resources and the Environment. The Working Group's activities included the international harmonization of our regulatory policies, questions of Federal support of research related to biotechnology and the eventual commercialization of the findings of this research. Working Group activities were housed in the Office of Science and Technology Policy (OSTP) in the Executive Office of the President and Dr. Bernadine Healy, then Deputy Director of OSTP, was the first working Chairperson. The Working Group was composed of representatives from approximately 18 agencies. As we described to this Subcommittee approximately one year ago, the Working Group focused primarily on questions related to regulation of biotechnology and the initial product was the December 31, 1984 publication in the Federal Register, of a proposed framework for the coordination of Federal policy for the regulation of biotechnology. That publication presented a "Regulatory Matrix" consisting of a compilation of the existing statutes which the Working Group felt were applicable to the products of biotechnology. In addition to the regulatory matrix agency statements were published from the FDA, USDA, and EPA regarding their respective proposed policy for biotechnology regulation. The Working Group statement also included a proposal for a coordinated Scientific Advisory Mechanism. Approximately three months after this original statement, the Occupational Safety and Health Administration (OSHA) separately published a similar policy statement outlining its approach to biotechnology related questions. The public was invited to provide comments regarding all parts of this proposed coordinated framework and many letters were received. A few details of the responses may be found in a recent Federal Register notice, published on November 14, 1985 (Federal Register Vol. 50, No. 220, pp. 47174-47195). The public comments reflected a very wide diversity of views which ranged from the extremes in either direction. The Working Group has examined these public comments carefully and the individual agencies are modifying their policy statements to reflect the positive and useful suggestions contained in those comments. The revised agency policy statements will be published in the Federal Register on approximately January 31, 1986.

A significant portion of the Notice of December 31, 1984 was devoted to the establishment of a mechanism for the coordination of the scientific review procedures and policies across the several agencies. A two-tiered structure was proposed, a lower tier consisting of the agency based advisory committee(s) and a second tier, or parent board, which would provide interagency review and coordination. At the first tier the research sponsoring agencies (NIH and NSF) and the regulatory agencies (USDA, FDA and EPA) would utilize their respective science advisory committees for outside guidance in answering scientific questions raised by applications for research funding or approval of product testing or marketing. However, the existing committees had been reviewed and deemed not adequate to fulfill the role of interagency coordination in an area as diverse as biotechnology.

Accordingly, a new committee, the Biotechnology Science Board (BSB), was proposed that would have been chartered by the Department of Health and Human Services, and reported to the Assistant Secretary for Health. The proposed board would have included members from each of the agency-based scientific advisory committees. It was proposed that this board have a broad authority which included a second tier review of agency decisions regarding the review of applications.

The comments to this proposal raised various concerns. Of the seventy-nine letters to OSTP, almost half dealt with the structure and functions of the BSB. Twenty-five comments reflected fears that the two-tiered structure was too cumbersome, and that the double review would impose unreasonable delay and become a disincentive to development of new products. Eight were concerned with the ability of the BSB to protect confidential business information. Sixteen letters expressed the view that the BSB should be established within the Office of the Assistant Secretary for Health and should be a "super-RAC", that is, a multiagency version of the successful NIH Recombinant DNA Advisory Committee (RAC). Seven letters expressed concern that the establishment of such a committee would detract from the strong and influential position of the present NIH RAC.

Other opinions were expressed that the BSB should set guidelines on policy for scientific review, but should not be a review board; should provide advisory but not binding reviews; should review applications only at the request of an agency; and should include ethical and social considerations in their reviews.

In light of these concerns, the Working Group considered many alternative models as modifications or replacements of the BSB. There remained consensus that interagency coordination of science questions resulting from applications of all types was desirable. However, there was also a consensus that there was no need for a second level advisory committee review. The Working Group agreed that a committee made up of officials from NIH, NSF, EPA, FDA and USDA could serve the required function and provide a forum for the exchange of information between these and other agencies as well as the public. Such a committee would include only federal officials, therefore scientific data contained in applications could be shared since confidential business information or other proprietary data could be appropriately protected. A coordinating committee of this type could also hold public meetings at regular intervals.

Following the decision to establish such a committee, its appropriate location was examined. HHS had been suggested for the BSB, however, several factors suggested that other locations should be considered. HHS contains within it two groups that would be members of the coordinating committee, NIH and FDA. Maintaining the committee within HHS might suggest an HHS point of view and open the question of rivalry between the new committee and the NIH RAC. After all of the factors were considered, the Working Group felt that a location away from any of the agencies directly involved would be the most appropriate, and the Office Of

Science and Technology Policy was selected.

The Federal Coordinating Council for Science, Engineering and Technology (FCCSET) appeared to be a suitable organizational location and structure under which to place the functions of the coordinating committee. Accordingly, a FCCSET committee was established to coordinate science issues related to research and commercial applications of biotechnology. The committee is called the Biotechnology Science Coordinating Committee (BSCC).

The charter of the committee established it as an interagency coordinating committee. To quote from the charter, the purposes of the BSCC are to:

> "Serve as a coordinating forum for addressing scientific problems, sharing information, and developing consensus;
>
> "Promote consistency in the development of Federal agencies' review procedures and assessments;
>
> "Facilitate continuing cooperation among Federal agencies on emerging scientific issues; and
>
> "Identify gaps in scientific knowledge."

The BSCC charter provides for the sharing of scientific information and authorizes the BSCC to seek and obtain all materials relevant to the details of an application and its handling by the agency. The BSCC is empowered to have periodic public meetings and to convene workshops, symposia, and coordinate special studies related to scientific issues in biotechnology.

The charter calls for the BSCC to be chaired by the Assistant

Director for Biological, Behavioral and Social Sciences of the National Science Foundation and the Director, National Institutes of Health on a rotating basis.

The BSCC has met and begun its work. The committee has scheduled meetings at approximately monthly intervals for the next several months and intends to continue this practice for at least the next six months. The first open public meeting is planned for February 14 and will be held in the auditorium at the National Academy of Sciences. I am very enthusiastic about the committee operations. Each member has clearly come with an attitude of open cooperation and mutual support. The discussions have been far-ranging and candid. While the committee does not have a mandate embedded in statute, each member has promised full participation through the signing of a Memorandum of Understanding which pledges full cooperation in the operations of the committee as set forth in the charter. The Committee structure was approved by the Domestic Policy Council and has that Council's support. This provides a basis of consensus at a very high level within the Administration.

It is important to note that the BSCC was established as a scientific policy and implementation committee and not a broad policy committee for the Administration. The policy considerations relating to biotechnology will remain the task of the Working Group. With the reorganization of the White House Councils, the Biotechnology Working Group was rechartered under the Domestic Policy Council. That Council has reviewed the

Working Group's activities to date and its plans for the future. The Working Group remains the primary forum for the discussion of broad policy topics related to biotechnology and to most aspects of interagency cooperation outside of the specific area of scientific review. While only experience will provide evidence for the full effectiveness of the BSCC mechanism, I am very confident that it will succeed. The Committee has already been useful in providing assistance to one of the member agencies during the process of a product review, and there is no reason to anticipate that this close collaboration will not continue.

On November 21 and 22, 1985 the National Science Foundation and the Office of Technology Assessment co-sponsored a workshop related to the horizontal transfer and stability of new genetic material introduced into the environment. The panel was composed of eighteen scientists recognized for their expertise in ecology, plant biology, population biology, molecular biology and related fields and included government, university and industry scientists. The workshop was open to invited outside observers and over the period of the two days at least 40 observers from congressional staff, government agencies, professional societies, environmental groups and the press were present. It was a productive and stimulating meeting.

The goal of the meeting was to address a series of scientific questions related to the introduction of new genetic constructions into the environment. The primary focus was on the stability of such material and the probability and potential mechanisms of transfer of genetic material between different organisms. The discussion was relevant to both intentional and unintentional release of genetically modified organisms, although we focused on the intentional release question. In previous scientific meetings dealing with questions related to intentional release of organisms into the environment, the scientific community had been reluctant to draw any generalizations regarding the effects of such introductions. Initially the NSF/OTA meeting was no exception, with the majority of the participants focusing on the gaps in our knowledge rather than on those areas where we have some understanding. As the meeting developed throughout the first day, however, the amount of data sharing was considerable and the focus of the attention changed. By the second morning, the panel was willing to try to develop some generalizations which could be used to guide regulators and legislators alike. I would like to use the resulting framework to describe a possible approach to the examination of an intentional release and then to go on to discuss some of my personal impressions based on the panel's discussions and conclusions. One factor dominated the discussions even when potential guidelines were being discussed: there was general agreement that, at the present time, each application must be judged on a case by case basis. However, there was also general agreement that not all intentional environmental releases would have the same potential impact.

The following "decision tree" became the working model for the assessment of potential environmental applications of the products of biotechnology.

I. Is there a potential hazard?
   A. Is this a "new" organism or a new application of a naturally occurring organism?
   B. Is this a new genetic construction in the organism under consideration and if it is what is the normal distribution of the new genetic information?

II. What is the probability of transfer of genetic material to new potentially hazardous organisms?
   A. What are the known mechanisms of genetic transfer within the newly engineered species?
   B. What is the frequency of transfer within this species and what might be the consequences of transfer of the information (i.e., the new phenotype)?
   C. What is the probability that the transferred material will be expressed and is there likely to be a positive selection for the new phenotype if transfer and expression did occur?
   D. What are the environmental factors which might influence known gene transfer mechanisms?
   E. What are the possible countermeasures that may be used to prohibit genetic transfer?
      1. Alternative vector systems.
      2. Alternative genetic constructions
      3. Mechanisms of biological containment

It must be stressed that the workshop and this outline which resulted from it, were not envisioned to be fully comprehensive but instead to focus on a limited number of questions about which we had some information. It is representative of the type of information currently available within the scientific community but which is generally not available in the form best suited for application to regulatory questions related to intentional release of genetically manipulated organisms into the environment. One of the results from the above analysis is that it is necessary to immediately differentiate between different groups of organisms. While gene transfer between unrelated bacteria is widely known, such horizontal transfer between unrelated plants is almost unknown and when it does occur the results are dramatically different than in microorganisms.

Participants in the workshop used this outline to analyze several of the potential biotechnology products currently under investigation by industry. Generally the panel was convinced that the particular applications discussed did not pose a hazard within themselves but that it would be undesirable for the genes in question to be transferred to a new species. By following the outline through section II, it was possible to identify a series of questions of critical importance to the regulator. As I stated earlier, it was very clear at this point that the species of the released organism and the species of the potential target(s) were the critical factors. It was widely felt that non-sexual horizontal gene transfer between genetically-modified and native plants was of such a low probability as to be negligible. The potential hazard posed by transfer in plants is even less than may be imagined when it is remembered that the transfer will occur only between plant cells and that this would not likely change the geneotype of the entire plant, nor is it likely to enter the pollen grains of these plants, especially if male sterility is introduced into the plant at the same time. Therefore, the panel concluded that the only potential hazard posed by genetically modified plants was from the environmental effects of the new gene product itself and not from the fact that recombinant DNA technology may have been used to derive the new plant variety.

With genetically modified microorganisms the situation is somewhat different. There are several known mechanisms for gene transfer in bacteria and they are present in different forms in different species. Therefore, it is essential to identify the potential target(s) of a transfer which could possibly lead to undesirable effects and then to analyze the possible countermeasures that may be used. It was agreed that the existing technologies within modern molecular biology have provided for extremely effective countermeasures for many applications. It must be remembered that the countermeasures must work in a wide range of environmental situations in addition to the original site of application and any potential selective advantage for a new construction must be taken into account. The net result is that the reviewing regulator must balance the mathematical probability of a transfer event with the mathematical probability of favorable environmental and selective conditions. In so doing, we will reach the boundaries of our knowledge, but is also likely that many of the envisioned applications will easily fall within those boundries and can be examined confidently within our present body of knowledge.

During the discussions at the workshop, we explored the nature of the information available regarding horizontal gene transfer, microbial ecology and evolutionary biology. The NSF Program Officers who were on the planning committee and participated in the workshop used this opportunity to develop a series of research questions that might be explored in the future. For the benefit of the Subcommittee and others who follow the debate regarding regulation of biotechnology, I would like to provide a generalized list of research topics for the future. This list is principally focused in the area of evolutionary biology, population biology and ecology but participation by the molecular biology community will be essential. Representative topics include:

1. What are the ways in which the ecology and evolutionary biology of microbes are substantially different, perhaps even unique, relative to other organisms and how must our current theory be modified to reflect those differences;

2. Since most current microbial research is done with organisms maintained under optimum laboratory conditions, how can we learn to extrapolate from laboratory results to realistic statements about what should be expected under field conditions;
3. How can we better define conditions under which horizontal transfer can occur and what environmental factors might control the rate;
4. How can we most effectively determine the natural history of a given microbial species including its population size, generation time and seasonal variation in the field;
5. It is very clear that species identity is maintained even in the presence of multiple mechanisms of horizontal gene transfer and we must learn more about how this identity is maintained over many thousands of years even in closely related microbes which may occupy the same ecological niche;
6. How much must we change an organism before it no longer can fill its normal niche and at what genetic level (i.e. gene, plasmid, chromosome or individual) must we examine selectional advantage; and
7. How does population structure effect the rate of evolutionary change and the potential for modification through horizontal gene transfer?

It is my opinion that the participants left with a much broader range of exciting questions than those just presented, and I expect that we will see greater attention in these areas in the future. It should be stressed that this is a broad research agenda designed to lead to a deeper understanding of microbial ecology and evolution. The answers to these questions would be of value to the regulator, but they are not essential for the regulator to effectively assess questions regarding the introduction of genetically modified organisms into the environment.

I came away from the workshop with two concerns regarding the debate over the intentional release of modified organisms. First, it appears that many people view genes as infectious agents which, if given the chance, will spread throughout the environment infecting a wide variety of organisms. We know, of course, that this is not true. Genes are simply fragments of DNA which must be within a living cell in order to be duplicated and, that once within that cell, will most likely stay there. Second, it is not uncommon for people to view microorganisms in the environment as simply the wild brethren of our laboratory subjects. We view them as happy and well fed, waiting to take advantage of any and all new opportunities. In reality, life is much more difficult. Soil organisms, for example, divide on the average of twice per year and survive in a state of constant starvation. They are not physiologically well prepared to accept or incorporate new genetic material even if it would provide them a new capacity for growth.

If the incorporation of that new gene involved production of a non-essential product, such as a pesticide, it is even less likely to ever occur.

We view this workshop as the first of a series devoted to specific areas of the broad topic of the environmental release of genetically modified organisms. At the present time we have two additional workshops planned and have discussed additional meetings with the National Academy of Sciences and others.

Mr. Chairman, thank you for this opportunity to testify before the Subcommittee. I would be delighted to answer any questions that you may have.

Mr. Wyden. Thank you, Dr. Kingsbury. Let me proceed with some questions now for Dr. Kingsbury, if I might.

Dr. Kingsbury, it seems quite positive in its charter the BSCC has the authority first to conduct analyses of broad scientific issues that go beyond those of any one agency; second, to come up with generic scientific recommendations that can be applied to recurring situations; third, to convene workshops, symposia, and generic research projects relating to scientific issues in biotechnology.

How do you and Dr. Wyngaarden expect to use these provisions to promote methods development?

Mr. Kingsbury. The committee is a small group of high level administrative people who have, because of the nature of the interactions within the committees, developed a good working relationship at a very professional level.

We are able to openly discuss questions of the appropriateness and nature of how an agency goes about its business to make recommendations to each other, to suggest scientific research topics, and I think within that context, we will be able to take the information that comes back and to develop a series of recommendations and a series of generic guidelines based on experience, based on research findings, and to, through these senior people, incorporate them in the review process within the agencies.

Now, not only is the committee of seven going to be operating, but there will be a series of subcommittees that will deal with some of the very substantive issues and report back to the parent BSCC, as well. And those subcommittees will have a wider involvement of agencies that are involved with this activity.

So, we see a broad base of material being developed. We see it coming to the committee, which has, in part, through its good working relationship, the ability to incorporate that information.

Mr. Wyden. Doctor, I have been concerned about some of the apparent limits to the authority of the BSCC. Now, the charter, of course, says the BSCC is authorized, and I quote here, "to develop generic scientific recommendations that can be applied to similar recurring applications."

But what I would like to know is, what is your authority to insist that the agencies have adequate science available to approach risk assessment in a unified way?

Mr. **Kingsbury.** We have no statutory authority to do that, but what we do have is the—as I mentioned in the testimony—the agreement of all of the members of the committee to participate and abide by the recommendations of the committee.

We have the opportunity to deal with the agency review committees to have a discussion of a particular issue that might come up, and I think, finally, as I pointed out in the testimony, at this time, the committee has a high profile within the administration. So one can always go—because it is within the Domestic Policy Council—one, if necessary, could deal with the secretaries of the particular agencies or the administrator.

I believe that we—because of the nature, the committee will rarely, if ever, have to do that. But it is a consensus committee. It is not a committee that has statutory background that can force people to do things. There is no question about that.

Mr. **Wyden.** Well, Doctor, I am pleased that the BSCC may prove to be a scientific guiding light for methods development.

But I am also concerned about a related problem, and that is that so little seems to have been accomplished since our hearing a year ago to remedy the inadequacies of the scientific basis for making regulatory judgments, and if agreed upon methods are the only way short of statutory changes to reduce statutory conflicts, it just seems to me that the administration hasn't invested very much in the effort to avoid regulatory delay and confusion.

This is the same year, after all, in which the applications for field experiments are coming to the agencies for approval of the first releasing of genetically engineered organisms.

Now, I think the point I want to make clear is that I don't hold you personally responsible. In fact, to the contrary, I think it is widely held that you have been one of the few consistently active scientific policy makers.

But I just have to note the dramatic effects of the absence of leadership in HHS, where there has been no Assistant Secretary of Health for a year, and we hear there will be a change at the secretarial level, as well. In addition, since Dr. Healy left OSTP, and Dr. Keyworth has annonced his resignation, leadership from OSTP also seems to be in a state of flux.

It is just my view that this combination of forces doesn't serve the public very well, and it is difficult to clarify public policy when the key decisionmakers aren't even identified, where you can't find out who is in charge.

I just must say this only heightens my concern of leaving such extremely critical matters to the discretion of the executive branch, and I know that this subject is going to be discussed again, as well, and want you to know of my concerns and the subcommittees.

Mr. **Kingsbury.** I would like to make a couple comments about that. I thank you for your kind comments. I believe, however, I would like to really address two points.

Let me address the second point first. I think that one should not ignore the fact that the interest in biotechnology, the interest in the regulation of the matrix and really interest in additional questions regarding biotechnology, questions of commercialization, questions of federally funded research—these are very serious issues not being dealt with at the science advisors level.

I was invited not long ago to attend and made a presentation to the Domestic Policy Council, which is chaired by the Attorney General, to describe the working groups activity and to outline for the Domestic Policy Council what our activities will be over the next year and the kinds of agendas that we see as being functional beyond the regulatory matrix.

And really, those focus on two issues, questions regarding commercialization, which we think are important issues. And we must come back to the notion of what we are trying to do here and that is to make the commercial world rational.

Second—and I think it is germane to your questions—is that research agenda must be coordinated. At one time during the past year, shortly after we appeared here, we initiated a subcommittee on research within the working group, and we were collecting data on the levels of research activity in the different agencies and the type of research, and that collection was done in a computer-based matrix to identify subject areas.

We were interested in two issues. One is could we predict the kinds of regulatory questions that we were going to be seeing in the agency a year, two years, down the road; and second, could we make an assessment of how adequately we were approaching the data base to support the regulatory work, now. This brings me to the final point, and I think all of us who are in the science funding agencies believe we don't have enough money, and we are not funded well enough.

I mean, one has to—you have to believe that before you can get through your oral exams to get your Ph.D. It is one of the first cuts that one makes. It is sort of a religion that goes with the science.

But what I would like to point out is, in fact, during this year there has been a dramatic change in the science associated with examining questions of deliberate release and microbiology.

I think the NSF/OTA workshop recently was an example of the heightened interest and, I think, was the high point of the year in terms of bringing new information together and focusing on what was needed.

If you will remember, I believe Mr. Sikorski handed me a year ago a document from a meeting that was held in Cornell which was a group of ecologists who were just doing their first things, you know, this was their first long shot at the whole issue.

I think we have come a very long way since then. There have been a series of coordinated meetings. The research agenda at the National Science Foundation has been modified in the BSR division.

To reflect the need for this information, the increased activity, so I would like to make the argument that it is not quite as abysmal as it may seem on the surface.

The scientists are quiet people, and we are just out there studying these little microbes and trying to stay out of the papers and off the television.

Mr. Wyden. Scientists, if I might interrupt, are quiet people, but you have been exceptionally eloquent, and it is just our concern that we really have that coordinated research agenda that you have said is so essential, and with all these vacancies and all these positions seeming to be in a state of flux, it just seems to us movement has not been what it might.

But you—and the budget cuts is an additional factor. But we——

Mr. Kingsbury. I remain eternally optimistic.

Mr. Wyden. And we are optimistic because there are people like you on the front lines trying to put in place a more coordinated research effort, and Chairman Dingell could not be here again this afternoon, but it is a subject of great interest to him that we make these scientific judgments in a rational way, and to do that we have to coordinate the research agenda. We very much appreciate your comments. I didn't mean to interrupt you.

Mr. Kingsbury. That is fine. I was finished.

Mr. Wyden. We will try not to have you in the papers all the time.

Dr. Moore, if we might have some questions for you, because we know you have a great deal of experience with methods development as well.

Now, as I understand it, the scientific experience from toxicology demonstrates the assessment of a risk of a particular organism or product is based, in part, on the predictive test run in the laboratory or as field tests, and for biotechnology, even where the statutory standards may differ, these scientific methods for predicting behavior of organisms in a particular environment will be the same for all statutes.

So we might understand a little bit more about how these tests are developed and validated, can you tell us about the methods development process for toxicology that was used at the program when you ran the National Toxicology Program?

TESTIMONY OF JOHN A. MOORE

Mr. Moore. Thank you, Congressman.

I would be glad to. My background is in toxicology, I do think the approaches that were used in pursuit of toxicology methods development or refinement validation certainly are general approaches to the scientific community that have equal application to coming up with risk assessment in the area of biotechnology.

Let me give you an example. The current methodologies that we all use today in this country as well as elsewhere in the world for trying to predict the ability of, say, a chemical to cause birth defects, basically rely having to do extensive animal studies that are not only very time consuming, but very expensive.

We all, I think, would like to have some surrogate measure that would allow one to screen lots of chemicals and then to focus the time-consuming animal studies on those that are deserving of greater study. Such a method doesn't exist. However, out of basic research institutions several years ago came two different studies identifying cell culture systems that the authors felt had predictive use in this area.

These studies were very provocative and indeed caught our attention as well as others. But to take something from that stage of being reported, by in this case, a basic scientist in North Carolina and one in Boston, to the stage of being able to apply it on a routine basis to make judgments as to risks that might be associated with a given product requires that those methods be put in somebody else's hands to see if they can make them work.

If they indeed do make them work, I think we then have what is often what I call the tedious, boring part of methods development evaluation. One then has to select a universe of chemicals. In the example I am giving, say, three or four different chemicals, some that are known to cause birth defects as well as some not know to cause defects, would have to be coded, and placed in the hands of laboratories to see if the methanol will work with a broad universe of chemicals.

Once that has been done, you have a data base available to determine whether this method has predictive utility, or that it has predictive utility only under a certain set of circumstances. It is this latter tedious part of the effort I think is sometimes to interest the scientific community in performing.

Mr. **Wyden**. Doctor, can the same approaches be used in microbiology and ecology to develop the predictive tests and describe the consequences of introductions?

Mr. **Moore**. Yes. No question. Obviously, you end up with different systems, but the approaches are usually generally the same.

For example, somebody may say that in my laboratory I have studied a certain organism which may be a good surrogate for possible ecological effects if it is a water contaminant. Other people have to take that and apply the same type of methodological approach I just talked about.

The other thing I think we have to do in trying to come up with predictive modelings for ecological effects is to get agreement within the scientific community as to what are bacteria, or other organisms that will appropriately serve as the surrogate, if you will, for predicting what may well happen in the field trials. To the degree we have those available, we all are fairly comfortable as to what their strengths and limitations are.

They then will have utility in screening products from an R&D standpoint and allow us to have greater confidence in the decision process that leads to allowing some of these R&D efforts to proceed to the field trial circumstances.

Mr. **Wyden**. Doctor, the subcommittee has gotten detailed responses from each Federal agency involved in biotech research. We asked exactly how much of this R&D was being done to aid the regulatory decisions. And I think you wouldn't be surprised to learn that there is very little.

You would agree that more such methods development needs to be done in the future?

Mr. **Moore**. My experience has been that there is a lot of basic research that is being done for specific reasons by the scientist who is dreaming up and getting funding for it. I think a regulatory agency's responsibility is to keep track of what those studies are; to be alert to whatever the goals of the individual scientists might be, to see what practical utility may they also have, for a regulatory agency in trying to assess possible environmental effects of products of biotech; and to seize upon those to the degree that gaps seem to be existing, again using a BSCC type of mechanism to funnel back into the funding agencies. He could then say we would like to see something else in this area, and in some selective circumstances with a limited budget that EPA may have compared to some of the other budgets in the Federal Government for this type of work, to use it primarily, I think, as a gap-filling type of exercise.

Mr. WYDEN. Do you think the new BSCC can assist the agencies in developing a unified methods development agenda?

Mr. MOORE. Yes, sir. As Dr. Kingsbury described a few minutes ago, the subcommittee that was put together earlier this year can effectively pool research needs and requirements of various agencies. What he then alluded to certainly impacted what NSF is doing in the way of funding. In a similar vein, we can have that same impact from an NIH standpoint, and maybe from some of the more targeted research programs of the USDA.

Mr. WYDEN. Dr. Moore, in addition to doing new research, it ought to be possible to apply the results of completed research.

Now, the National Science Foundation and OTA just completed a symposium of just this sort, didn't they?

Mr. MOORE. Yes, sir. There was one about a month ago, I believe.

Mr. WYDEN. Dr. Kingsbury, I am sure you would agree additional conferences by OTA and NSF would be useful.

If funds were available, how much such programs do you think could be undertaken each year for the next several years?

Mr. KINGSBURY. It is not clear how one would most efficiently divide the broad questions of environmental release up. In fact, we have begun the process of trying to attempt that particular thing. I would envision our agenda incorporating approximately a half a dozen such conferences a year, at least for the next year, and perhaps on past that.

It is my impression that there is a limit to how many of these should be NSF and OTA sponsored. Certainly, I believe that after this series is held and perhaps a few others—as I mentioned, we have plans now to fund two other such conferences that will not meet with OTA—I would like to see a consensus composite type meeting at the National Academy where all of the workshop results are brought together.

Mr. WYDEN. Doctor, if OTA were to have a budget to pay for these kinds of conferences, I gather you think that would ensure that this important job got done more quickly. Otherwise, we would have to wait for NSF or others to come forward, or——

Mr. KINGSBURY. The NSF-OTA workshop that was held in November was jointly funded. But there is a limit to how many of that type of activity—the types of things that we can do at that level, and I am sure that it would in fact have a very positive impact, and I think——

Mr. WYDEN. If OTA——

Mr. KINGSBURY. If OTA—and I think also would give a clear message to them of what the expectations were, and we would work together.

Mr. WYDEN. If I might come back to this coordination question just for a second, Doctor, in terms of using the BSCC to coordinate biotechnology research efforts, maybe you could tell how this could be done in three separate research areas, this kind of coordination function. Why don't we start in terms of the risk assessment studies?

Mr. KINGSBURY. OK——

Mr. WYDEN. In fact—I'm sorry, let me tell you what the three are. One would be risk assessment studies, second would be studies which are related to risk assessment, and third orphan products. What we are looking at is essentially trying to see how you would handle the coordination issue.

Mr. KINGSBURY. OK.

The risk assessment area, which you asked about first, has several parts to it, and one part is the generic notion of how one approaches a scientific risk assessment activity. What that really means, what are the bases for that. I think that we are in the process now of defining many of those things.

There is an interagency group outside of biotechnology, a much broader group that is an NSF-OSTP joint activity that is really addressing those questions, and this has been in place now for about a year, so it has some indirect effect back onto the BSCC, because it is generating generic information. And it is addressing a series of assumptions that one makes when one does risk assessment.

In the absence of any real hard information, one makes assumptions that are based on the best information available, and we are trying to step back and ask some questions about are the assumptions that have been made in the past valid and what we can do about it.

Second, there are a series of things that go on in different agencies that are related directly to biotechnology. The National Science Foundation has been involved in those and there is recently a publication that was a joint publication by the Arthur D. Little Co. and NSF that had wide distribution and that information has been shared. A copy of that report was the first document, I believe—I think I'm absolutely accurate on this—was the very first document that was circulated between the members of the BSCC.

So as a result, as these materials come available, we are doing the best we can to circulate them, to open discussion. We are asking for criticisms, we are asking for areas where different agencies see the questions that they need to have answered, brought up in a different way. I have learned a great deal over the last year about the kinds of questions that my colleagues at the EPA need to ask when they undergo a risk assessment analysis. It is much different than what I would have originally anticipated. Those kinds of data sharing exercises have been very valuable.

At the same time, a similar activity goes on at the scientific level, not just at the broad risk assessment level, but when one finds specific findings they are shared in a similar fashion.

I think the orphan drug issue is one we have not dealt with within the BSCC at this point. We have not met that many times that we have gotten that far down on our agenda. We are still focusing on getting these regulated properly and keeping everything under control.

Again, that is a forum. I think the orphan drug issue actually is the type of issue that would be dealt with more appropriately in the working group, in the Cabinet Council working group, because it is really, I think, more of a policy level issue than it is a scientific issue.

The Cabinet Council working group will continue to play the central policy role for biotechnology. The BSCC is really trying to focus on the scientific questions, and as that becomes a policy question, then it is dealt with that way. But in the broad sense, it is trying to stay away from policy-oriented kinds of activities.

The working group very legitimately would answer such questions as orphan drugs, intellectual property, things of that sort, when the tax laws are appropriate for stimulation of certain kinds of R&D activities.

Mr. WYDEN. Well, let me make one technical observation here. The Chair observes that Dr. Wyngaarden was unable to be here in person today, but has expressed an interest to enter answers to written questions in the record. Let us order the record be open for answers to written questions for Dr. Wyngaarden and anything else appropriate.

[The information referred to may be found in subcommmittee files.]

Mr. WYDEN. Having taken care of that, Dr. Kingsbury, let me talk about another couple of areas with you.

First, with respect to training of competent regulators, I think all of us would acknowledge the need for sufficient number of well-trained scientists at regulatory agencies to make and review decisions for the release of the genetically engineered organisms.

In your view, what kind of training is needed?

Mr. KINGSBURY. Well, from my point of view, I would like to have the scientific staff that are dealing with these questions have training in really three areas right now. I think that it is important to separate different agencies and what their focal points should be.

The FDA, as a regulatory agency in research related to biotechnology and products related to biotechnology, really takes a much different view and has an agenda that is quite a bit different than what Dr. Moore is dealing with at the EPA.

I think the classic approach of someone who can interpret the appropriate clinical information and toxicological information at the FDA really continues to be appropriate. I think the types of people they have had are appropriate to the biotechnology world. I really don't see that this is a particularly different area and I believe that Dr. Young agrees with that.

In the EPA world, we are looking at a series of questions of complex, genetically engineered constructions, again back to the notion of one tries to engineer in a poison-pill type of defense against environmental spread or something of that sort, and then the regulators need to have the molecular biology background to understand what has been done as well as the ecological background and the basic training in methods of risk assessment that I think are appropriate to any regulatory agency.

Mr. WYDEN. Do we know that enough scientists with the appropriate training are available now?

Mr. **Kingsbury**. I think that Dr. Moore can probably answer that better because he has done more recruiting in that area than I have.

Mr. **Wyden**. You are the one out there saying, "We want you."

Mr. **Moore**. Congressman, we have yet to, I would say, experience a concern over the lack of adequate numbers of personnel at this stage and time.

I might also point out the number of demands that are being placed upon us are fairly modest. We have not yet received any applications, for example, relating to regulation under the Toxic Substances Control Act.

In the last year we had several types of inquiries relating to the development of a pesticide through biotechnology capability. So it is still relatively modest.

I anticipate, and I think everybody else anticipates, that sometime in the future, the number of products that are going to be reaching the stage of commercialization is going to grow logarithmically, and indeed, the ability of the Agency to keep pace with demand is still something that is speculative.

While we all know it is going to increase, I am not sure any of us are confident in predicting when that is going to happen.

Mr. **Wyden**. Dr. Kingsbury, have you and your alternate chairman of the BSCC, Dr. Wyngaarden, discussed the scientific agenda that you have laid out today?

Mr. **Kingsbury**. Yes. We have had a couple of chances to get together and discuss the philosophy of the BSCC operation and the agenda and how we should approach a series of questions as to what we should bring to the table, what we should bring to the discussions, and how we should approach a whole variety of issues, including the subcommittees.

One of the things that Jim and I have had an opportunity to discuss is what the subcommittee structure should look like to most functionally now provide us the kind of depth that we would like to have to back up the BSCC.

Mr. **Wyden**. By and large, are you and Dr. Wyngaarden in agreement?

Mr. **Kingsbury**. We have been in complete agreement on all of these issues, and let me say, he is not here, but I hope you do not interpret that as a lack of interest on his part.

Mr. **Wyden**. No.

Mr. **Kingsbury**. I have been very enthusiastic about the level of his involvement and his level of interest. He believes this is a very important committee, and has taken a great deal of interest.

Mr. **Wyden**. So the Congress might assume continuity when Dr. Wyngaarden assumes the chair?

Mr. **Kingsbury**. I believe you will not know there has been a difference.

Mr. **Wyden**. Some questions with respect to surveillance and enforcement for both of you, if we might.

Since scientists first expressed concern about the consequences of introducing new genetically manipulated organisms, or genetic material into the environment, I think everybody acknowledges that we have made a lot of progress.

First in NIH established voluntary guidelines for the researchers. Then they required Federal grantees to follow the guidelines.

We also learned that the risks were less grave. Now the Departments of Agriculture, Health and Human Services, and Labor and EPA are writing rules to extend Federal review to private actions. I trust we can expect safe practices from firms that apply to these agencies and comply with the rules.

Now, Dr. Kingsbury and Dr. Moore, there is another concern and that is the failure of some researchers and industrial firms to comply with the rules perhaps even inadvertently. Would you agree at this point there is no enforcement and surveillance mechanism in place to tell us whether genetically engineered organisms are escaping into the environment at present?

Dr. Kingsbury.

Mr. KINGSBURY. I do not know of a mechanism whereby we can monitor every biotechnology firm in the United States to find out if they are inadvertently releasing products. I think that what one has to do is rely on the fact that good manufacturing practices and responsible operation of the company requires that these guidelines be followed, but at this point we do not have a policing system that is in effect.

It is possible that that can be done and the water people at EPA certainly monitor other plant effluents, and I would expect they could monitor this one.

Mr. MOORE. Congressman, two thoughts come to mind. Most of the effort that is going in the use of biotechnology today I would say is still in the R&D stage as opposed to the advanced commercial relations stage.

My experience as a member of the scientific community is that scientists are very, very sensitive to what their colleagues think of them. For example, the peer pressure or peer review probably as effective a means to make sure that one does comply with the concept if not the specificities of say, the NIH guidelines, or points to consider in the way of a policing action.

On the other hand, some in the scientific community may not want to hasten commericialization by circumventing the rules or speeding up the process. The other thing that I think would be a hindrance toward anybody who might even entertain such thoughts is that sooner or later if they are planning to develop something for commercialization they have got to bring their data to Federal regulations. To the degree they are developing something outside the rules, there is no way that they are going to want to bring that data to me some time down the road.

Mr. WYDEN. Well, gentlemen, I guess it just seems to me this is a problem that we have got to figure out a way to address.

My concern is that the systems don't exist right now to catch those who break the rules and clearly it is my view that we have got to address this in the future and we want very much on this subcommittee to work with you to figure out an effective way to do it. But I think it is something that clearly must be looked at in the future.

One other area. We have been talking about the problem of accidential and unreported releases but we would like to also ask about how it is proposed to monitor the long-term consequences of the releases that are approved, and specifically how will Federal agencies in the BSCC handle these decisions?

Mr. **Moore**. I could comment on the one experiment that we have approved. That was the ice-minus experiment with AGS. We approved one single experiment. If they want to do subsequent experiments they must come back to the Agency and get our permission. We also are sharing with our colleagues what it was that we did in the process of approving that. We also put in some specific requirements as a conditon of approval.

One, in the case that we have approved we did state they must notify us 15 days before commencement of the experiment so that we do have the opportunity to have an EPA representative there.

Second, with respect to that experiment there also was some concern about the need to try to capture data as to air dispersion of the bacteria.

In this instance the company expressed a willingness to allow such data to be captured as part of the experiment but lacked the necessary equipment if you will, to do the air monitoring. EPA possesses such equipment, so in this instance we indeed are going to use EPA equipment to capture such data.

The other thing we have done, and I think will continue to do with this experiment and future experiments at least in the near term, is to require that indeed those conducting the experiment do provide EPA results of all those experiments because I think that the result of those experiments are going to allow us collectively to be better informed in passing judgment on the next experiment that comes down the road.

Mr. **Kingsbury**. These are—this kind of surveillance is not something that is unique right now, and Dr. Moore's comments about the monitoring of micro-organisms in the air around these experiments brought into my mind the fact that a couple of years ago, there was an experimental irrigation system set up, I believe it was in Arizona that was using wastewater and that was going to be using wastewater in an area where it was going to be sprayed rather than just down an irrigation canal.

I am not sure if it was the State of Arizona or if it was the Federal Government that required this kind of monitoring over a long period of time in that particular setting.

It comes to mind because he just pointed out not everyone has that equipment. It happened the research institute that I was director of at that time had one of the largest accumulations of this kind of air sampling equipment that was available, and we made it available to them to be able to do these kinds of studies.

It is possible to build on that data base so it is not something that is uniquely new to just biotechnology today.

Mr. **Wyden**. Let me recognize minority counsel for any questions I may want to pursue.

Mr. **Wilson**. Thank you very much, Mr. Chairman. I have a couple of questions. Dr. Kingsbury, I understand you have an extensive background in the development and science of biological warfare. Can you describe that background for us?

Mr. **Kingsbury**. Well, I was director of a research institute called the Naval Biosciences Laboratory, which, in the 1950's—prior to my directorship, I might add—was involved in aerobiology and other topics related to the biological warfare effort that existed prior to the 1972 ban.

At that time, that institute discontinued all of that kind of work, but some of that expertise remained there, but there was no work of that sort going on.

Mr. WILSON. This morning, Dr. Richard Novick made a number of points about the issue of the potential for military or terrorist uses of biological weapons.

Dr. Novick expressed concern that surveillance or control over these uses is inadequate. Based on the background you have described, and your knowledge and experience, are the points that Dr. Novick made serious threats; and if so, how should these concerns be addressed?

Mr. KINGSBURY. Well, it is my feeling that the U.S. Government had clearly taken the position in 1972, and it is my understanding, although I couldn't document this for you today, that President Reagan just recently reaffirmed his position that biological weapons are outside of the sphere of interest of the United States, and he has no intention of having any work on biological weapons done in the United States.

And to the best of my knowledge, there is none of that kind of work going on. There are a variety of projects that are currently being funded. All of them have come through the Congress, I believe, as line items mainly from the U.S. Army's Medical Research and Development Command for defensive—mainly detection and some vaccine development.

But that is the closest thing that I know of to anything that one would call developing biologics.

Mr. WILSON. Do you believe a line can be drawn between offensive and defensive in the area of biological warfare research?

Mr. KINGSBURY. I believe that is possible. The reason is as someone who over the last number of years has been interested in studying the virulence of micro-organisms and running into the extraordinary complexity that genetic engineering, as powerful as it may be, really is not the kind of magic bullet that would provide us the kind of insight to do engineering for offensive purposes.

It is very easy to use this kind of biotechnology to get a microorganism to produce an antigen for a virus. You can get E.coli or yeast to produce a glycoprotein from a paramyxo-virus or related virus, and use that as an antigen to immunize people.

That is vastly different than engineering a micro-organism that has the appropriate properties or pathogenecity one might want to use as a weapon. That is a complex thing, depending on—one of the things that was learned in the 1950's and 1960's is that the factors that influence an appropriate biologic are extraordinarily complex, and there are those who may want to be a bit cynical who said one of the reasons we gave up and were so willing to sign the ban is because the thing didn't work in the first place. Based on my experience, I would have to say that is possibly true.

Mr. WILSON. Does the increasing development of biotechnology in general significantly increase the threat or possibility of the use of biological weapons?

Mr. KINGSBURY. There are technologies available through biotechnology to do things that we hadn't thought about before, or to do things in a unique way. I think that it would be foolish for me to try to say it is impossible to use biotechnology to do weapons, you know, weapons in the very broadest sense.

Certainly, it could be done. It is possible to clone bacterial toxins into micro-organisms in an unusual way. It is possible to clone a variety of other kinds of perhaps pharmacologically active agents in a unique way.

So, to say that this wouldn't be possible would be foolish.

Mr. **Wilson**. I have one question for Dr. Moore.

Dr. Moore, do you believe that the current case-by-case approach to building a base of knowledge for overall regulation is the best way to proceed?

Mr. **Moore**. I think the case-by-case approach is the only appropriate mechanism to use at this stage of our evolution.

On the other hand, I would hope that sometime in the future, based on the experience that we have gleaned from this case-by-case approach, we might be able to then get into generic application or more general approaches on certain types of classifications. I think that is what we are all probably looking for, to supplant the case-by-case approach.

We certainly don't want to be using the present case-by-case approach in 1995 and 1996.

Mr. **Wilson**. Can an adequate data base be developed to make predictions about the consequences of the release of biologically engineered organisms without studied experimental releases? I would ask that of both you gentlemen.

Mr. **Kingsbury**. I don't believe so.

Mr. **Moore**. I would concur with that.

Mr. **Wilson**. Thank you very much, Mr. Chairman. I have no further questions.

Mr. **Wyden**. Thank you.

One additional one for you, Dr. Kingsbury. It is my understanding that USDA is completing a review for approval of a field test of a herbicide-resistant tobacco species developed by the Calgene Co. When Calgene first sent its application to APHIS, the regulatory branch of the USDA, APHIS said they did not have, in effect, the authority to regulate organisms that are not plant pests or plant pathogens. They sent the application back to Calgene.

Now, again it is my understanding that Calgene had to persuade the Agriculture Secretary, Mr. Block, to accept the application for review by USDA, and this looks to me like it would really be a problem area, for the time being, at least.

You know, it is important that the field tests be subject to scrutiny and regulation. I think what the subcommittee would be interested in is, how will the Federal Government handle these kind of situations in the future?

Mr. **Kingsbury**. As you are very well aware, the Agriculture Department has had a long history of dealing with new crop varieties, of examining a whole series of issues of the development and introduction of new varieties. They have had a mechanism and it has been extremely effective. This has been done through a multiple-tiered mechanism.

But it has also been clear, I think, in the last year, as you point out, that that mechanism, as good and as beneficial to U.S. agriculture as it has been, has not been quite adequate to deal with the fast-changing agri-biotechnology. They recognize that, and we have been working very carefully and very closely with the Agriculture Department to try to assist them in every way we can to be able to identify the experts in the field that they need to help them put together their appropriate advisory review committees and to streamline this process in a way that makes it very effective and gives the level of scientific review that we all would like to see.

This has actually been a focus of the domestic policy council working group until now, with the BSCC, certainly, was one of the topics at our first BSCC meeting. We continue to be supportive of them. We continue to provide staff assistance to the development of their guidelines in the review of their mechanism. We think we are coming a long way.

I think that what you have described as a problem, that I have heard about before, and we have identified as a problem, that we really wanted to help them solve, they have been very cooperative in accepting our help.

Mr. WYDEN. I hope so. APHIS, they don't have the authority to regulate in these kinds of situations, and it sure strikes me as unnecessarily cumbersome and again not a very coordinated way to go about doing these things.

Is there a need for a new statute in this area?

Mr. KINGSBURY. I don't believe there is. There is simply a need for the Department of Agriculture to recognize where their communication problems have been and what the technology demands, and have them now really focus on this. I believe they are doing that.

Mr. WYDEN. Gentlemen, if you don't have any further comments, you both have been very patient. I think it is my feeling, having sat through now about 5 hours' worth, even though the mechanism and the structure of what needs to be done seems to be moving very slowly, we are glad that people like yourselves are willing to think in a thoughtful way about these kinds of issues, and hopefully Congress can help you in your work and help speed up some of the things that need to be done.

I know Chairman Dingell has a great interest in trying to make this subcommittee of assistance to all of you, to put that mechanism and structure in place, and we will look forward to working with you in the days ahead.

We thank you for your participation with the subcommittee. If you don't have any further comments today, we will excuse you.

The subcommittee is adjourned.

[Whereupon, at 3:15 p.m., the subcommittee adjourned.]

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